TO STUDY THE CLINICAL AND ETIOLOGICAL PROFILE OF EPILEPTIC SPASMS IN CHILDREN

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I hereby declare that the thesis entitled **"TO STUDY THE CLINICAL AND ETIOLOGICAL PROFILE OF EPILEPTIC SPASMS IN CHILDREN"** submitted towards partial fulfillment of the requirements for the award of **MD IN PAEDIATRICS** degree to BFUHS is a compilation of original work carried out by me under the supervision of **Dr. Jatinder Singh Goraya,** Professor, Department of Paediatrics & **Dr. Siddharth Bhargava,** Associate Professor, Department of Paediatrics. No part of this thesis has formed the basis for the award of any degree previously.

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Dedicated

to

my Family

&

Teachers

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Dr. Amneet kaur

LIST OF ABBREVIATIONS

- **AIIMS** - All India Institute of Medical Sciences
- **CT** - Computed Tomography
- **CNS** - Central Nervous System
- **EEG** - Electroencephalogram
- **HIE** - Hypoxic Ischemic Encephalopathy
- **HMG CoA** - Hydroxymethylglutaryl- coenzyme A
- **IS** - Infantile spams
- **ILAE** - International League Against Epilepsy
- **LSCS** - Lower segment Cesarean Section
- **MRI** - Magnetic Resonance Imaging
- **NVD** - Normal Vaginal Delivery
- **NHBI** - Neonatal Hypoglycemic Brain Injury
- **PVL** - Periventricular Leucomalacia
- **PEHO** - Progressive Encephalopathy with edema, hypsarrhythmia and Optic atrophy.
- **TSC** - Tuberous Sclerosis
- **UKISS** - United Kingdom Infantile Spasms Study

ABSTRACT

BACKGROUND: Epileptic spasms**,** previously termed as infantile spasms are still a cause of significant morbidity in children. Spectrum of disorders associated with epileptic spasms has undergone substantial change over time. There are several western studies describing the etiology and clinical profile of epileptic spasms, but only fewer Indian studies focused on this subject.

AIMS & OBJECTIVES: To study the clinical and etiological characteristics of epileptic spasms and to assess the spectrum of electroencephalographic and neuroimaging findings in children with epileptic spasms.

MATERIALS & METHODS: Prospective observational study of children older than one month of age, presenting with epileptic spasms to the department of Pediatrics at Dayanand Medical College & Hospital, Ludhiana, from March 2021 to September 2022.

RESULTS: Total of 41 children, 34 males and 7 females were enrolled. Age of onset of epileptic spasms ranged from 4 months to 3.5 years of age (mean 12 months). The mean time of presentation was 16 months. Flexor spasms (82.9%) was the commonest type. Most (82.9%) spasms occurred on awakening, and 95% children had additional symptoms. Other type of seizures accompanied epileptic spasms in 24.4% children. Perinatal illnesses were causative in 33 cases (80.5%). Only 1 case had normal development prior to onset of spasms and 73.2% cases had developmental regression or slowing after the onset of spasms. Microcephaly was the commonest neurological finding noted in 31.7% cases. All children had hypsarrhythmia on EEG including 2 cases (4.9%) with modified hypsarrhythmia. Periventricular leukomalacia (24.4%) was the most common MRI finding, followed by hypoxic ischemic brain injury in 22% cases. Structural – acquired cause was found in 70.7% cases, structural- genetic in 4.9%, genetic in 1 (2.4%), and no obvious cause was identified in 9 cases (21.9%).

CONCLUSION: Preventable perinatal risk factors like hypoxic ischemic brain injury and neonatal hypoglycemic brain injury are still the leading causes of epileptic spasms in our country. This highlights the need of improvement in antenatal services, perinatal and neonatal services in the country.

KEYWORDS: Epileptic spasms, infantile spasms, hypsarrhythmia, west syndrome.

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KEY TO MASTER CHART

- ✓ **EEG** - Electroencephalogram
- ✓ **AF** - Anterior Fontenelle
- ✓ **HIE** - Hypoxic Ischemic Encephalopathy
- ✓ **LPV** - Leaking Per Vaginum
- ✓ **LSCS** - Lower Segment Cesarean Section
- ✓ **NAD** - No Abnormality Detected
- ✓ **NVD** - Normal Vaginal Delivery
- ✓ **NHBI** - Neonatal Hypoglycemic Brain Injury
- ✓ **PVL** - Periventricular Leucomalacia
- ✓ **MRI** - Magnetic Resonance Imaging
- ✓ **MSL** - Meconiom Stained Liquor
- ✓ **UTI** - Urinary Tract Infection
- ✓ **WES** - Whole Exome Sequencing

INTRODUCTION

Epileptic spasms (infantile spasms) were first identified by William James West in his own son in 1841, as a peculiar kind of infantile convulsions.[1] Also called “salaam convulsions”, the entity came to be recognized as infantile spasms in the literature. The International League Against Epilepsy (ILAE) 2017 operational classification of seizure types, now uses the term epileptic spasms in place of infantile spasms.[2] The term “epileptic spasm” is now preferred over infantile spasms as spasms can present for the first time beyond infancy period.[3] Defined as sudden flexion, extension or mixed extension-flexion of predominantly proximal and truncal muscles.[2] Electroencephalographically, epileptic spasms are marked by the presence of “hypsarrhythmia”.[4]

Epileptic spasms are characterized by abrupt tonic contraction lasting for a few seconds mainly involving the muscles of the neck, trunk, and limbs with abduction or adduction of the arms. The type of convulsion in epileptic spasms depends on the muscle groups involved (flexor or extensor) and on the extent of the contraction. Flexor spasms are the most common type of epileptic spasms.[5-8]

The Epileptic spasms may be accompanied by episodes of cry, scream or even smile/laughing, which may precede or follow the spasm itself. The spasms appear mostly in rapid sequence and occur prevalently on awakening and uncommonly just before sleep. In the most severe ictal phenotypes, the spasms may be noticed also during sleep. Affected children after the crises may be irritable or may have drowsiness.[5-8]The onset of spasms is sometimes so subtle that it is often missed by parents. The cry associated with it may be misinterpreted by the physicians and parents alike as infantile colic![1] Children may present with infantile spasms alone or in combinations of West syndrome.[9] Latter is an epileptic encephalopathy characterized by the triad of infantile spasms, usually clustered; hypsarrhythmia on electroencephalogram (EEG), with tracings

showing a chaotic, multifocal and bilateral pattern of high-amplitude waves; and psychomotor regression. [10]

Variants of this classical presentation comprise variations of age of onset, ranging from the first month to 4 years, spasms that may be asymmetrical or combined with focal seizures, asymmetrical, synchronous or fragmented hypsarrhythmia, and psychomotor function which may be delayed, deteriorated or normal. These variations mainly seem to depend on etiology, and specific patterns have been identified for the various causes.[11]

Hypsarrhythmia was defined as EEG Showing high voltage chaotic slow waves intermixed with spike and sharp wave discharges. Modified hypsarrhythmia was defined in presence of any of the following: increased interhemispheric synchronization consistent voltage asymmetries; consistent focus of abnormal discharge; episodes of generalized/regional or lateralized voltage attenuation; or primarily high-voltage bilaterally asynchronous slow wave activity.[12]

Most of the children presenting with epileptic spasms have either psychomotor development regression or slowing. Developmental delay at presentation with infantile spasms might be due to the epileptic encephalopathy having been present prior to the presentation. More often it is due to underlying neuropathology, mostly of perinatal onset brain injury. Children who develop infantile spasms frequently have preexisting brain damage which may however only be recognized following identification of epileptic spasms. Rarely, epileptic spasms are recognized on specific questioning in a child who has developmental delay.[13]

Epileptic spasms, though long recognized, are still a cause of significant morbidity in children. The knowledge of their etiology and pathogenesis is still evolving. Recognized as an age-related epileptic encephalopathy, epileptic spasms have onset between 3 months and 2 years with an estimated incidence of 0.2 to 0.5 per 1,000 live births per year. It is most frequent form of epilepsy in infancy except neonatal and

febrile seizures.[14] The number of affected children by this condition is consistent over time and no increase has been recorded in the most recent population-based and case series .[15,16]

Epileptic spasms remain etiologically heterogeneous. The etiology is identified in 60 to 75% of cases with relevant radiological, infectious, metabolic and genetic investigations.[13] Often, an obvious etiologic distinction is not strictly feasible, since different events may concur in causing the epileptic spams. In about 20- 35% of cases, the etiologic event remains unknown: the outcome, in these cases, is usually more favorable as compared with the group with recognizable etiologies.[17]

Etiologically, epileptic spasms constitute an age specific epileptic encephalopathy associated with many different underlying neurologic conditions. Perinatal hypoxic ischemic brain injury is recognized as the commonest acquired cause of epileptic spasms. Other adverse perinatal events such as meningitis, encephalitis, metabolic brain injury secondary to hypoglycemia, inborn errors of metabolism, congenital TORCH infections are also recognized antecedents of epileptic spasms. Of the genetic etiologies, chromosomal disorders, tuberous sclerosis, malformations of cortical development such as lissencephaly, polymicrogyria, focal cortical dysplasia, schizencephaly, and other complex brain malformations are known causes of epileptic spasms. [1,11,14]

With the advent of next generation sequencing, an increasingly number of genes are being identified to as being associated with epileptic spasms in infants and children.

Spectrum of disorders associated with epileptic spasms has undergone significant change over time, attributed to large extent to advances in neuroimaging and genetics, and improved perinatal care. In developed countries, contribution of perinatally acquired brain injury to the causation of epileptic spasms has diminished and that of genetic factors increased. Advances in neuroimaging and genetic techniques has made it possible to recognize increasing role of genetic factors in the etiology of

epileptic spasms in these countries. Previously classified as symptomatic, and idiopathic/cryptogenic epileptic spasms now are classified along with other epilepsies as being structural, genetic/presumed genetic, infectious, metabolic, immune or unknown etiologies. [1,11,14].

In developing countries such as ours, obstetrical, perinatal and neonatal care still remains suboptimal, perinatal brain injury remains as the most common cause of epileptic spasms in infants and children.[3,18-21] As a result, perinatal risk factors continue to be the dominant cause of epileptic spasms. [2,21-23] In addition to hypoxic ischemic encephalopathy , potentially preventable perinatal causes of neonatal brain injury such as hypoglycemia is being recognized as the most common cause of perinatally acquired etiology of epileptic spasms in Indian children. Paradoxically, genetic factors are also being recognized increasingly, attributable to better availability and affordability of next generation sequencing as well as to improved access to expert pediatric neurological services across the country.[21]

Aim of the current study was to evaluate the spectrum of etiologies underlying epileptic spasms in the current era of changing pre-natal, perinatal and neonatal care and availability of advanced neuroimaging, molecular and genetic investigations in our country.

AIMS AND OBJECTIVES

1. To study the clinical characteristics of epileptic spasms in children.
2. To determine the etiological profile of epileptic spasms in children.
3. To assess the spectrum of electroencephalographic and neuroimaging findings in children with epileptic spasm.

REVIEW OF LITERATURE

Epileptic (infantile) spasms were first described by JH West in 1841 in his own son who was healthy until 4 months of age when he developed *bobbings* of head which progressively increased in frequency and severity to cause complete heaving of head towards his knees. The child also suffered from psychomotor retardation.[22]

About 100 years later, Gibbs et al. in 1954 described the characteristic electroencephalographic pattern called hypsarrhythmia associated with infantile spasms. It was described as chaotic and disorganized background activity with asynchronous large amplitude slow waves mixed with single or multifocal spikes and slow waves followed by voltage attenuation. [23]

Since then, a large amount of scientific literature has accumulated describing clinical, electrographic, neuroimaging, etiological, therapeutic and prognostic characteristics of this peculiar disorder. The triad of epileptic (infantile) spasms, hypsarrhythmia on electroencephalography, and psychomotor deterioration is known as West syndrome, and represents one of the most common catastrophic epileptic encephalopathy with adverse outcome for development and seizure control. [14]

Epileptic spasms are peculiar kind of age specific epileptic seizures seen during early months of life. Onset of epileptic spasms is during the first years of age in vast majority of the cases with 94% cases occurring within 12 months of age. The most common age of onset is 4–6 months.[24] Occurrence beyond 3 years is extremely uncommon. Slight male predominance has been observed in several studies.[14] In a study by Surana et.al. male to female ratio of 3.3:1 was noted.[21] Brna et al. in their study suggested that the observed male predominance reflects the predominance in males in the referring population. An alternate explanation is the increased complication rate of common etiological conditions, such as neonatal hypoglycemia and hypoxic ischemic encephalopathy reported to occur more frequently in male infants.[25,26]

The Epileptic spasms may be flexor, extensor or mixed but the flexor spasms are the most common. [1,2,14] Accounting for 42% cases in a study by Khreisat et al. flexor spasms were the most common type, followed by mixed spasms in 36% cases and extensor spasms in 22% cases. [27] In an Indian study of 148 children, flexor spasms were noted in 76.3%, mixed spasms in 17.6% and extensor spasms in 6 % children.[18]

Spasms can be easily misinterpreted by parents or physician, especially when consisting of flexion of lower limbs on the abdomen, as "abdominal colics". Spasms can be asymmetric and can additionally be associated with partial or generalized seizures. Autonomic symptom such as skin flushing, sweating, pupillary dilatation or changes in respiratory or heart rate can be present.[28,29] Epileptic spasms can also present with features such as yawning, gasping, isolated eye movement and transient focal motor activities, clinical significance of which has been reported as unknown but they occur in the context of classical EEG pattern of Infantile spasms –hypsarrhythmia.[30]

Cyanosis, pallor, eye deviation and or change in respiratory pattern may be associated with the motor spasms before, during or after the attack. Cry or scream may precede or follow the ictal phase. As observed by West in his original description, Spasms usually occur in clusters; approximately 80% of spasms occur in clusters.[22] Studies have shown that there is little diurnal variation in frequency of spasm/cluster over a 24 hour period. However, spasms do not occur in sleep but occur most frequently on awakening or just before sleep.

Epileptic spasms even in clusters can be present without EEG findings of typical or modified hypsarrhythmia with or without focal paroxysmal discharges on the EEG and normal metabolic and imaging findings. In the study by Caraballo et al., out of sixteen patients, fifteen showed that epileptic spasms may occur in infancy without hypsarrhythmia. All sixteen patients also presented with clusters of

epileptic spasms and focal and generalized clinical and/or EEG abnormalities.[31]

Epileptic spasms are frequently associated with psychomotor retardation. Developmental regression or slowing after onset of spasms is a well documented phenomenon.[10] Yuskaitis et al., in a study of 133 infants with epileptic spasms of unknown origin, reported normal development in 15% vs. clinically well-documented developmental delay in the remaining 85%.[32]

The causes of IS may have their origin in the prenatal, perinatal, and post-natal period. In United Kingdom Infantile Spasms Study" (UKISS) study (2010) of 207 infants with epileptic spasms, proven etiology was identified in 61% children. Hypoxic ischemic encephalopathy was the most common etiology and was observed in 21 (10%), followed by chromosomal aberrations in 16 (8%), brain malformations in 16 (8%), stroke in 16 (8%), tuberous sclerosis complex in 15 (7%) and periventricular leukomalacia/ hemorrhage in 11 (5%). Miscellaneous and uncommon etiologies were diagnosed in 32(15%) children.[13]

Similarly, in another prospective multicenter study of 251 children with epileptic spasms, an etiology was established in 161 (64%). Of these, clinical assessment and/or MRI identified an obvious cause in 138 (55%). A genetic cause was identified in 14%, genetic-structural in 10.0%, structural-congenital in 10.8%, structural-acquired in 22.4%, infectious in 2% and metabolic in 5% children. [6]

Karvelas et. al. (2009), described 80 children with infantile spasms, male (46) preponderance was noticed . 50 children (63%) had symptomatic spasms with disorders of cortical development being the most frequent cause followed by neonatal injury and tuberous sclerosis. Thirty children had a positive family history of epilepsy. The mean age at diagnosis was 7.21 ± 4.7 months. Thirty two out of 50 (64%) patients in the symptomatic group had hypsarrhythmia on their EEG at diagnosis.[33]

In a national childhood encephalopathy study of 269 children with epileptic spasms, it was found that 34% had antecedent factors which may have caused the spasms, the commonest of these were perinatal hypoxia in 38 cases and TSC in 16 cases.[34]

In a study by Khreisat et al. (2011), age of onset of infantile spasms ranged from 1 month to 1 year and 6 months (mean – 4.8 months). The mean time of presentation was 9.4 months. A male preponderance was noted (74%). Flexor spasms (52%) was the commonest. Other types of seizures also accompanied infantile spasms in 44% children. History of birth asphyxia was obtained in 48%, 3 (6%) had positive family history. Developmental delay was recognized prior to onset of spasms in 52%, microcephaly was the commonest associated problem, Imaging studies of the brain revealed abnormality in 18 patients. 78% patients were classified as symptomatic and 22% as cryptogenic. 12% patients had congenital anomalies of brain, history of birth trauma was present in 4 % patients, neurocutaneous markers were also present in 2 % cases.[27]

Study by Pooya et al. (2013), out of the 2500 patients registered with epilepsy, thirty-two patients (1.3%) were diagnosed to have West syndrome. Age of onset was 4.99 ± 3.06 months. Male to female ratio was 1:1. Nine (28.1%) were reported to have two or more seizure types and 23 (71.8%) had one seizure type (epileptic spasms). There was no developmental delay detected in two patients and in the rest, a mild to severe delay was noted. Electroencephalography showed typical hypsarrhythmia in 59.4% of patients and modified hypsarrhythmia or atypical presentations were seen in 40.6%.[35]

Kulsoom & Colleagues, studied 36 patients with epileptic spasms, developmental motor delay was observed in 89, flexor spasms were noted in 30.5% children and mixed type in 28%. Based on etiological classification, the most common cause among the symptomatic infantile spasms was hypoxic ischemic insult (32%), followed by post meningitic sequelae (13.6%) and perinatal stroke (13.6%). Two children had Inborn

errors of metabolism and one had tuberous sclerosis. Hypsarrhythmia (69%) was the most common EEG finding followed by modified hypsarrhythmia (31%). MRI was carried out in all patients; it was abnormal in 36%. Most common radiological findings were vascular events (ischemia/hemorrhage in 46%) followed by congenital brain malformations (23%).[36]

In a study of 410 children with epileptic spasms, Mean age at presentation was found to be 4.6 ± 3.5 months. Eighty percent children presented due to infantile spasms / seizures and 20% due to psychomotor delay / regression. Seventy-two percent patients presented at the age < 6 month and no patient presented after the age of 18 months. Spasm types were mixed (56%), flexors (24%), extensor (12%) and asymmetric (8%).Symptomatic group accounted for 58% cases and Cryptogenic 42%. Electroencephalography (EEG) showed hypsarrhythmic / modified hypsarrhythmic pattern in 82% and other forms of epileptic discharges in 18%. The remaining 18 % showed other forms of epileptic discharges.[37]
Only few Indian studies on epileptic spasms are available, and most of these studies predate the latest 2017 ILAE classification of seizures and epilepsies.[2]

A perusal of these studies revealed symptomatic etiology in more than 80% of the cases with preponderance of perinatal brain injury especially asphyxial hypoxic ischemic encephalopathy of infantile spasms.[3,18-21] This is clearly greater than of about 60% reported from the western countries.[6,13]

In a study by Kalra et al. (2001)**,** 94 children with epileptic spasms were studied. Male to female ratio of 2.8:1 was noted. Median age of onset was found to be 3 months and age of onset was 12 months. It was found that developmental status remained normal throughout in 10 out of 93 children (10.7%) who had epileptic spasms and delayed in 67 children (72.04%). A change in developmental status was seen in 16 children (17.2%). Prenatal factors were found as etiology in 66.6% and perinatal

insults were seen in 33.3%. Important causes were: cortical atrophy 39.4%, birth asphyxia 21.2%, tuberous sclerosis 15.1%, migration defects 6%, infarcts 6%, meningitis 3% polycythemia 3% and biotinidase deficiency 3%.[38]

Study from All India institute of medical sciences (AIIMS), New Delhi (2011) described 95 children aged between 1 to 5 years of age who presented with epileptic spasms. Symptomatic etiology was observed in the majority, accounting for 78 (82%) of the cases. Perinatal asphyxia and neonatal sepsis/meningitis were reported in 43 (45%) and 29 (30%) children with epileptic spasms. Neonatal jaundice requiring phototherapy or exchange transfusion was reported in 8/95 (8.9%). Other frequent risk factors were brain malformations in 9, tuberous sclerosis in 4, and perinatal stroke in three. CNS malformations included lissencephaly (2), holoprosencephaly (1), isolated corpus callosum agenesis (5). One child with presumed pyridoxine responsive seizures had partial agenesis of corpus callosum and lissencephaly. Other metabolic causes included phenylketonuria (1) and HMG CoA lyase deficiency. Co-morbidities found at the time of neurodevelopmental assessment included vision impairment 32/95 (33.7%), hearing impairment 12/95 (12.6%), autism 13/95 (13.7%), hyperactivity 4/95 (4.2%), and drooling 15/95 (15.8%). [20]

A Study by Singhi et al. from Chandigarh, North India, (2003) reported 165 children aged 1.5 month to 4.5 years who presented with epileptic spasms. Age of onset ranged from 1 month to 19 months. A male preponderance was noted (67.9%). Flexor spasms occurred in 74% children. Other type of seizures occurred in 31 children- these were focal (6%), generalized tonic clonic (8.5%) and others. Spasms occurred on awakening from sleep in 92% cases. Associated behavior changes were noted in 30 % cases. Adverse perinatal events were recorded in 59%. History of delayed cry and birth asphyxia was obtained in 26.1%, neonatal jaundice in 17%, neonatal seizures in 30.3% and neonatal sepsis in 23.6% of the patients. Developmental delay was recognized prior to onset of

spasms in 69.7% and after the onset of spasms in 27.9%. Only 2.4% had no significant developmental delay. Associated problems like microcephaly, visual abnormalities (squint, refractory errors, cataracts) and hearing problems were seen in 72.7%, 29.1% and 10.9%, respectively. Seventy-seven children had cerebral palsy of different types. Nonspecific developmental delay was found in 66 children. Tuberous sclerosis contributed to epileptic spasms in 13 cases. Hypsarrhythmia was seen in 44% children, generalized spike and slow wave abnormalities in 31%, focal discharges in 11%, burst suppression pattern in 7%; in 8 children the EEG was normal. Magnetic resonance imaging (MRI) was done for 77 children. MRI revealed periventricular hyperintensities in 33.8% of cases; cerebral atrophy in 21%, corpus callosal abnormalities in 7.9%, neuronal migration defects in 3% and structural malformations in 6.6% cases, respectively. In 20(12%) children, the MRI was normal.[19]

In recent retrospective study by Kaushik et al. (2013) of 148 children (120 boys) with epileptic spasms, almost two-thirds of the children had flexor spasms with the rest having mixed or extensor spasms with an average 10 clusters per day, with each cluster having 5 spasms. 13 children were small for gestational age. Etiological diagnosis was described in 122 (82%). Perinatal brain injury was identified in 81 (66%) children, with perinatal asphyxia being the dominant cause. Neonatal sepsis/meningitis (13), neonatal hypoglycemia (5), prematurity (3), kernicterus (1), and perinatal stroke (1) were the other perinatal etiologies. Postnatal causes included meningitis and meningoencephalitis in 14 children. Malformations of cortical development in 5, intrauterine infections in 2, tuberous sclerosis in 1 and inherited metabolic disorders in 2 were the other uncommon causes of epileptic spasms. Prior to the onset of spasms, developmental delay was present in 137 (92.5%) patients. Electroencephalography (EEG) findings were compatible with hypsarrhythmia in 63 (42.4%) children; and with modified hypsarrhythmia

in the rest (57.6%).[18] More than 60% patients in an another Indian study had perinatal insults as the cause of infantile spasms.[39]

In a recent study by Gupta et al. (2020), 61 children with epileptic spasms were enrolled. Mean age at onset of spasms were noted to be 7.5 months. Flexor spasms were the commonest (96.7%). Etiology could be ascertained in 51/61 children (83.6%) and unknown in 16.4% (10/61). Perinatal asphyxia (40.9%), neonatal hypoglycemia (14.8%), and neonatal meningitis (9.8%) were predominant causes among the children with known etiology. Prenatal causes were found in 7.8% cases and postnatal meningitis accounted for 6% of the cases. Moderate to severe developmental delay was observed in 55/61 children (91.8%). Fifty one (83.6%) out of 61 children had hypsarrhythmia on EEG while 10 (16%) had hypsarrhythmia variants.[40]

Nawaz et al. (2020) studied 33 children with West syndrome. Male predominance was found, 23 (69.69%) were males. Mean age at onset was found to be 8.12 months (1-36 months) and mean age at diagnosis was 13.46 months (3-58 months). History of consanguinity was found in 32 % children. Majority (87.5%) of children had flexor spasms. 2 children had extensor spasms and 2 had mixed type of spasms. Twenty out of 29 had microcephaly (68.96%). One child had dysmorphism. Only 2 children (6%) had normal development prior to onset of spasms. 13 children had hypsarrhythmia on EEG. Etiology was found in 23 (69.7%) children. Birth asphyxia was most common among symptomatic group and was found in 12 children (52.2%) Other common etiologies included, hypoglycemia in 4 (17.39%), and meningitis in 5 (21.73%) children. Among antenatal causes; CNS malformation (1), Neurofibromatosis (1) and tuberous sclerosis (1) were found. In 10 children, no etiology was found on history, examination and/or neuroimaging.[41]

Another recent study, by Gehlawat et al. (2021), 30 children with epileptic spasms were evaluated and a male predominance (70%) were noted. The median age at onset of spasms was 4 months. The median lag

time to treatment was 5 months. Eight children (26%) were premature, 2 (7%) were small for gestational age, history of birth asphyxia was present in 56%, neonatal encephalopathy in 62%. EEG findings were hypsarrhythmia in 13 (43.3%) children and modified hypsarrhythmia in 9 (30%) children. Most common MRI finding was periventricular leukomalacia (54.1%) followed by cystic encephalomalacia (13.8%), normal MRI (20.7%) and one had arrested hydrocephalus. [42]

While perinatal brain injury, especially asphyxial hypoxic ischemic injury continues to play a dominant role in the etiology of this devastating epileptic encephalopathy of epileptic spasms. Recent studies have found neonatal hypoglycemic brain injury also to be a very common cause. In a recent retrospective study of the 113 children with epileptic spasms from Jaipur India, authors were able to establish a definite etiology in 94 (83%) children. Unlike previous Indian studies, neonatal hypoglycemic brain injury emerged as the most common acquired cause of epileptic spasms and was identified in 40 (35%) children. Asphyxial brain injury was identified in 29 children and was the second most common perinatally acquired cause. Of importance is the finding of genetic etiology identified in 17 children including 5 with tuberous sclerosis and 12 non-tuberous sclerosis gene mutations.[21]

Genetics causes are increasingly recognized as a cause of epileptic spasms. Genetic causes can either be disorders of genomic imbalance (e.g. Down's syndrome, Palister–Killian syndrome, Williams syndrome or Miller–Dieker syndrome) or single gene disorders such as mutations in CDKL5, STXBP1, or ARX.[43] Metabolic etiologies are rare but also recognized as being causative of epileptic spasms Pyridoxine dependency, biotinidase deficiency, PEHO syndrome, mitochondrial disorders, molybdenum co-factor deficiency and non-ketotic hyperglycinemia have all been described.[44]

MATERIALS AND METHODS

This prospective, hospital based study was conducted in the Division of pediatric neurology, Department of Pediatrics, Dayanand Medical College and Hospital, Ludhiana over a period of 18 months from March 2021 to September 2022. Children older than 1 month of age attending the pediatric out-patient, in-patient and pediatric emergency services who were eventually diagnosed with epileptic spasms were included in the study.

Epileptic spasms were defined as sudden occurrence of flexion, extension or mixed, brief and synchronous movement of the head, trunk or limbs, and often occurring in clusters.[2] Epileptic spasms are characterized by abrupt tonic contraction lasting for a few seconds mainly involving the muscles of the neck, trunk, and limbs with abduction or adduction of the arms. Electroencephalographically, epileptic spasms are marked by the presence of “hypsarrhythmia”.[4]

Hypsarrhythmia was defined as EEG Showing high voltage chaotic slow waves intermixed with spike and sharp wave discharges.[12]

Following inclusion and exclusion criteria were employed:

INCLUSION CRITERIA:

- Presentation with new onset epileptic spasms.
- Age >1 month.

EXCLUSION CRITERIA:

- Past history of epileptic spasms (Children who have had epileptic spasms previously and which were treated and resolved but came back with epileptic spasms were excluded).
- Parents refusal to participate in the study.

Written consent was obtained from the parents of the children with epileptic spasms to participate in the study. The selected children meeting the inclusion criteria underwent detailed clinical evaluation. All children were subjected to detailed clinical history which included age at the onset of spasm, frequency of epileptic spasms, types of spasms, number of

spasms per cluster, duration of clusters, other types of seizures, presence or absence of developmental delay, perinatal details, family history and treatment history were noted in a structured proforma. Physical examination including head circumference, dysmorphism, neurocutaneous markers and detailed neurological examination were documented. Other findings, such as organomegaly if present were also noted.

Brain Magnetic Resonance imaging (MRI) & Electroencephalography (EEG) were done for all patients presenting with epileptic spasms. Other metabolic investigations such as metabolic and genetic studies were performed as indicated and allowed by financial constraints.

Data was described in terms of range; mean ± standard deviation(±SD), median, frequencies (number of cases) and relative frequencies (percentages) as appropriate. All statistical calculations were done using (Statistical Package for the Social Science) SPSS 21version (SPSS Inc. Chicago, IL, USA) statistical program for Microsoft Windows.

OBSERVATIONS & RESULTS

A total of 41 patients met the inclusion criteria and were enrolled in the study. The demographic and clinical characteristics of these subjects are described below:

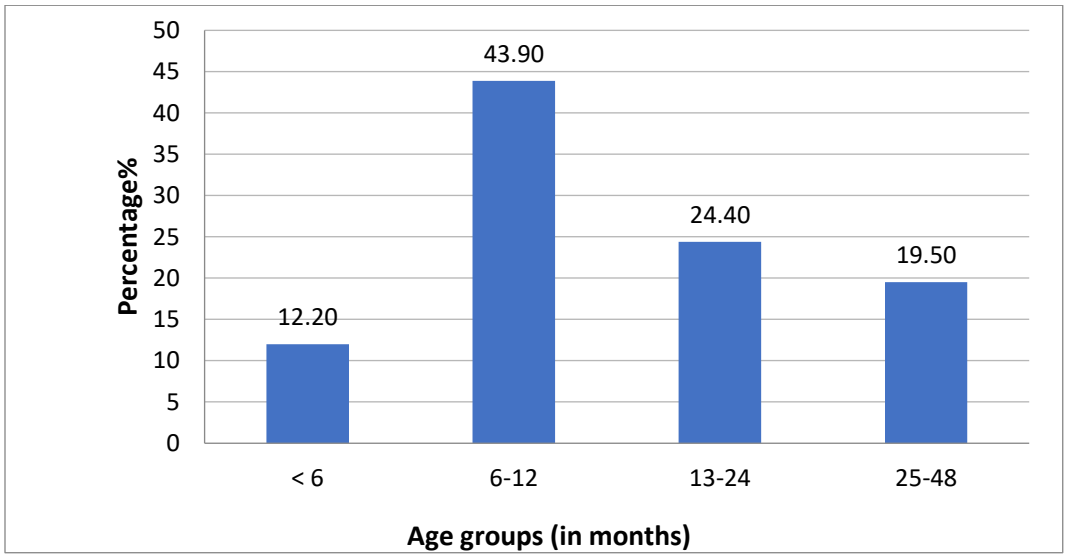
AGE AT PRESENTATION

Children age at presentation ranged from 4 months to 3.5 years of age. The mean age at presentation was 16 months. The age distribution of the subjects in the study group is depicted in Table 1 & Figure 1. Majority (80%) of the children were younger than 2 years of age.

Table 1: Age at presentation.

Age (months)	No. of cases	Percentage (%)
< 6	5	12.2
6-12	18	43.9
13-24	10	24.4
25-48	8	19.5
Total	41	100

Figure 1: Age group wise distribution in months at presentation.



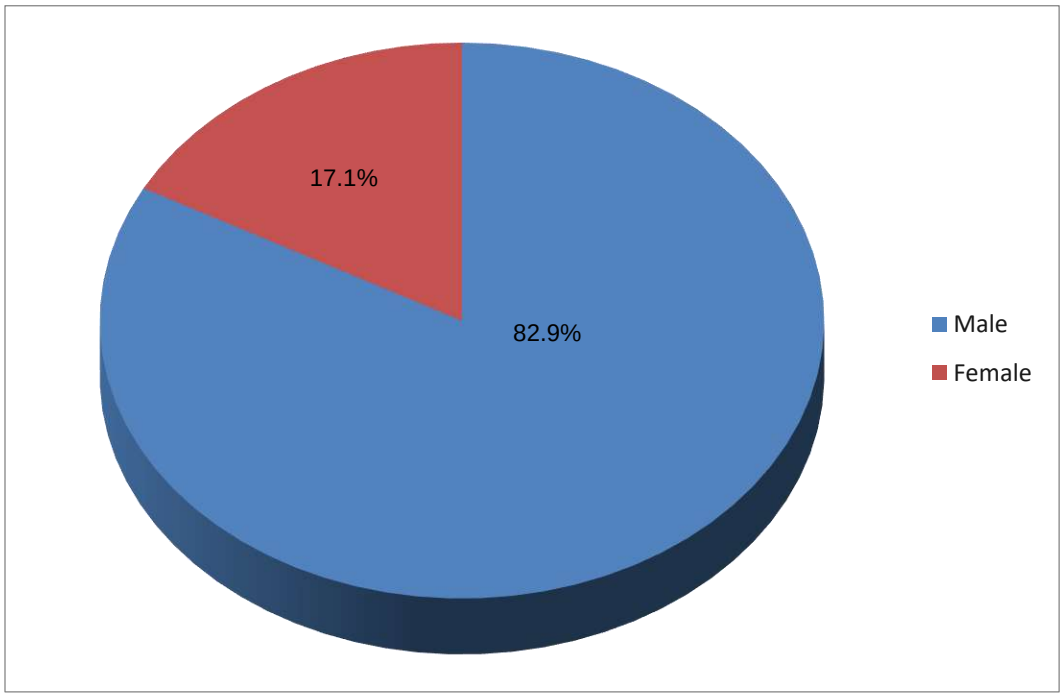
GENDER DISTRIBUTION

As shown in Table 2, 34 (82.9%) were males and 7 (17.1%) females. Male predominance was noted with male to female ratio of 4.8:1.

Table 2: Gender distribution of the subjects.

Gender	No. of cases	Percentage (%)
Male	34	82.9
Female	7	17.1
Total	41	100

Figure 2: Gender wise distribution of subjects.



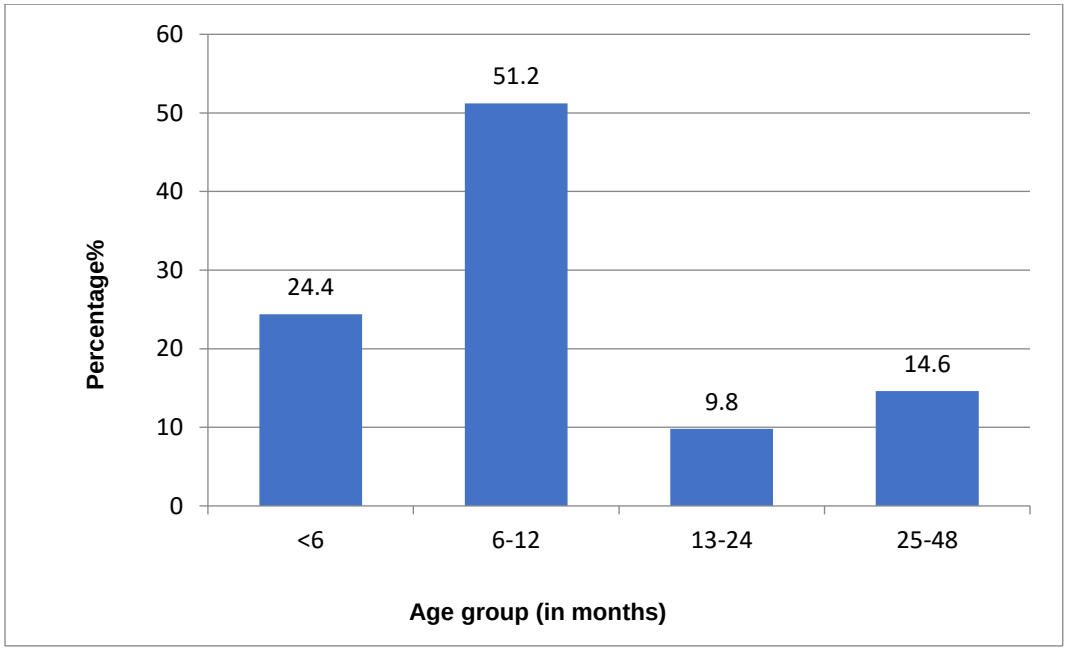
AGE OF ONSET

Age of onset of epileptic spasms was between 4 months to 3.5 years of age with mean age of 12 months. Majority (85%) were 24 months of age or younger at the time of onset of epileptic spasms. Only 6 (14.6%) children were older than 24 months at the onset of epileptic spasms.

Table 3: Age of onset of epileptic spasms.

Onset age (months)	No. of cases	Percentage (%)
<6	10	24.4
6-12	21	51.2
13-24	4	9.8
25-48	6	14.6
Total	41	100

Figure 3: Age of onset of epileptic spasms.



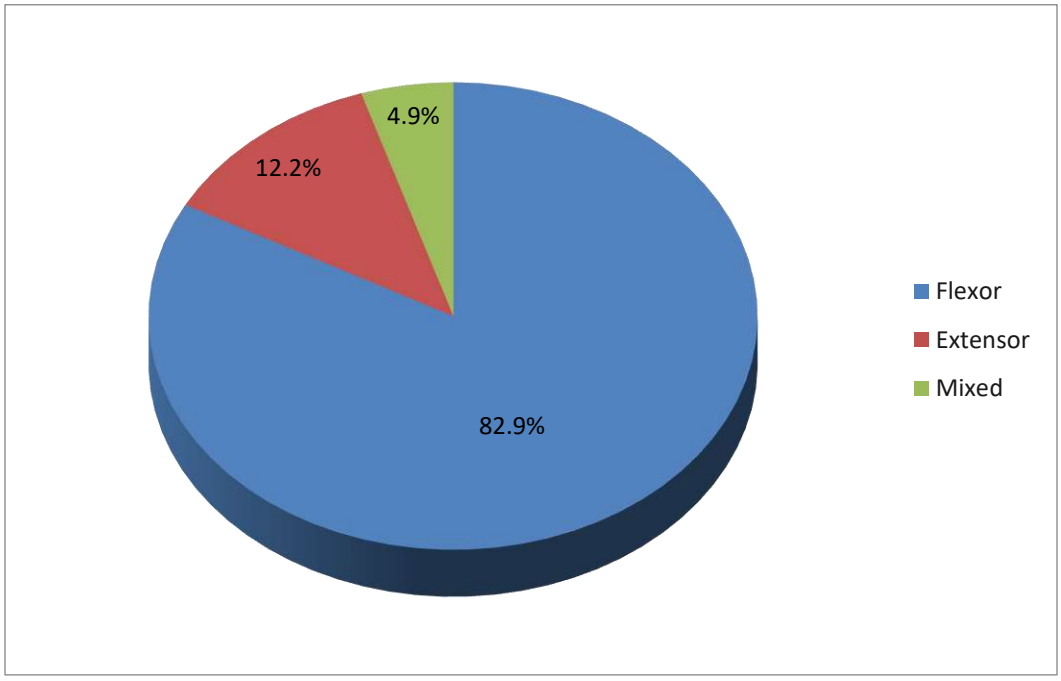
TYPES OF EPILEPTIC SPASMS

Flexor spasms were the most common spasms, noted in 34 patients (82.9%). Majority of the children 34 patients (82.9%) presented with flexor spasms, 5 (12.2%) had extensor spasms and 2 (4.9%) of them had mixed – extensor & flexor spasms. (Table 4 & Figure 4)

Table 4: Type of epileptic spasms.

Type of epileptic spasms	No. of cases	Percentage (%)
Flexor	34	82.9
Extensor	5	12.2
Mixed	2	4.9
Total	41	100

Figure 4: Types of Epileptic spasms.



CLUSTERING OF SPASMS

Clustering of epileptic spasms were noted in all the children.

NUMBER OF SPASMS PER CLUSTER AND DURATION OF CLUSTER

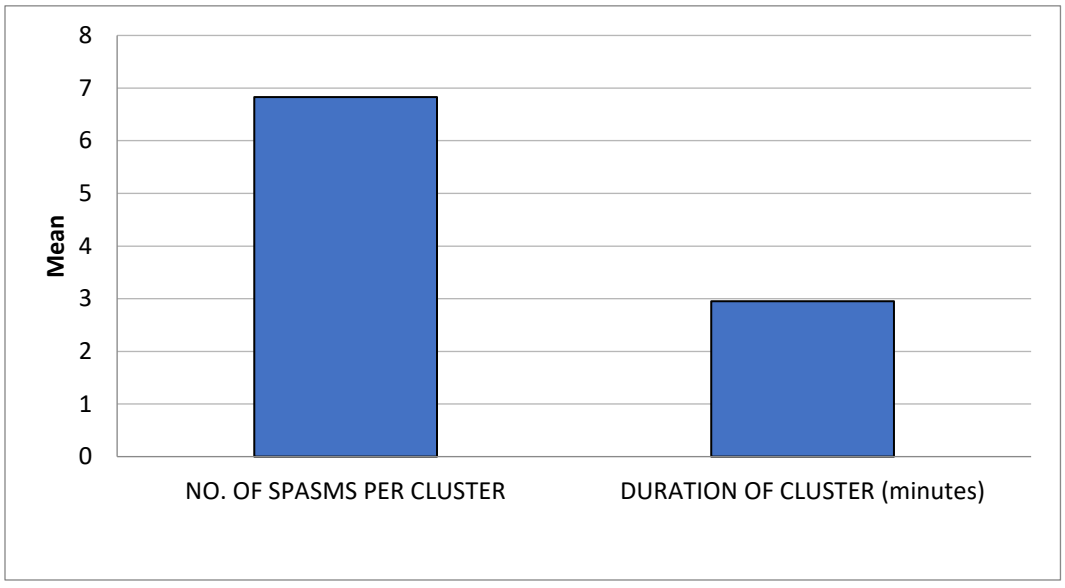
The maximum number of spasms noted per cluster was 20 and minimum of 2 with an average of 6 spasms per cluster, Range from 2-20.

The average duration of the cluster was 3 minutes with the range of 1-10 minutes.

Table 5: No of spasms per cluster and duration of cluster.

	N	Minimum	Maximum	Mean	Std. Deviation
No. of spasms per cluster	41	2.00	20.00	6.83	4.06
Duration of cluster (minutes)	41	1.00	10.00	2.95	1.82

Figure 5: No. of spasms per cluster and duration of cluster (in minutes).



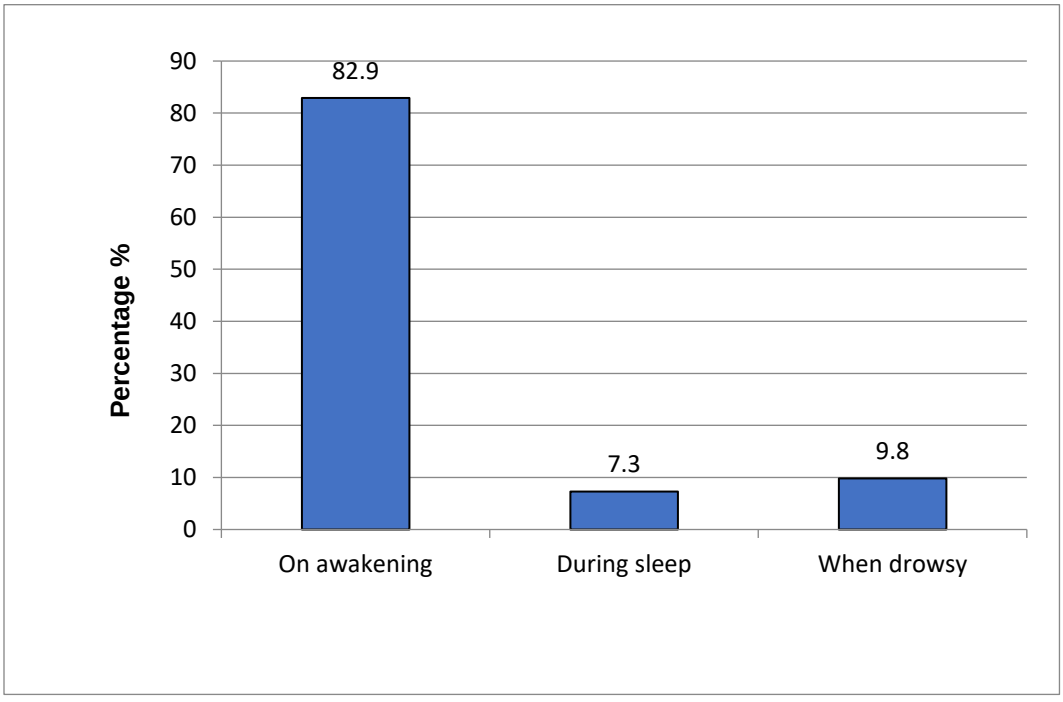
TIME OF OCCURENCE OF SPASMS

Out of the 41 children with epileptic spasms, majority 34 (82.9%) had spasms on awakening, 4(9.8%) had spasms when drowsy and 3 (7.3%) had spasms when asleep. (Table 6).

Table 6: Time of occurrence of spasms.

Time of occurrence of spasms	No. of cases	Percentage (%)
On awakening	34	82.9
During sleep	3	7.3
When drowsy	4	9.8
Total	41	100

Figure 6: Time of occurrence of spasms.



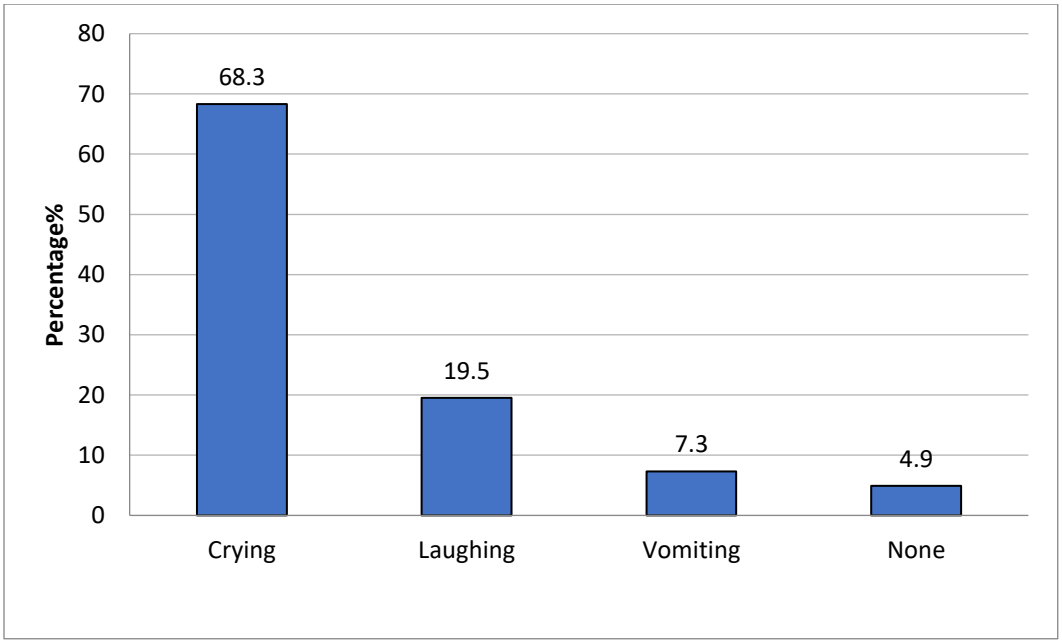
ASSOCIATED SYMPTOMS

Thirty nine (95%) children with epileptic spasms had additional symptoms in addition to motor phenomena. Twenty eight children (68.3%) with epileptic spasms had associated crying during the spasms episodes, 8 (19.5%) children had laughing, 3 (7.3%) children had vomiting (Table 7).

Table 7: Associated symptoms of epileptic spasms.

Associated symptoms	No. of cases	Percentage (%)
Crying	28	68.3
Laughing	8	19.5
Vomiting	3	7.3
None	2	4.9
Total	41	100

Figure 7: Associated symptoms with epileptic spasms.



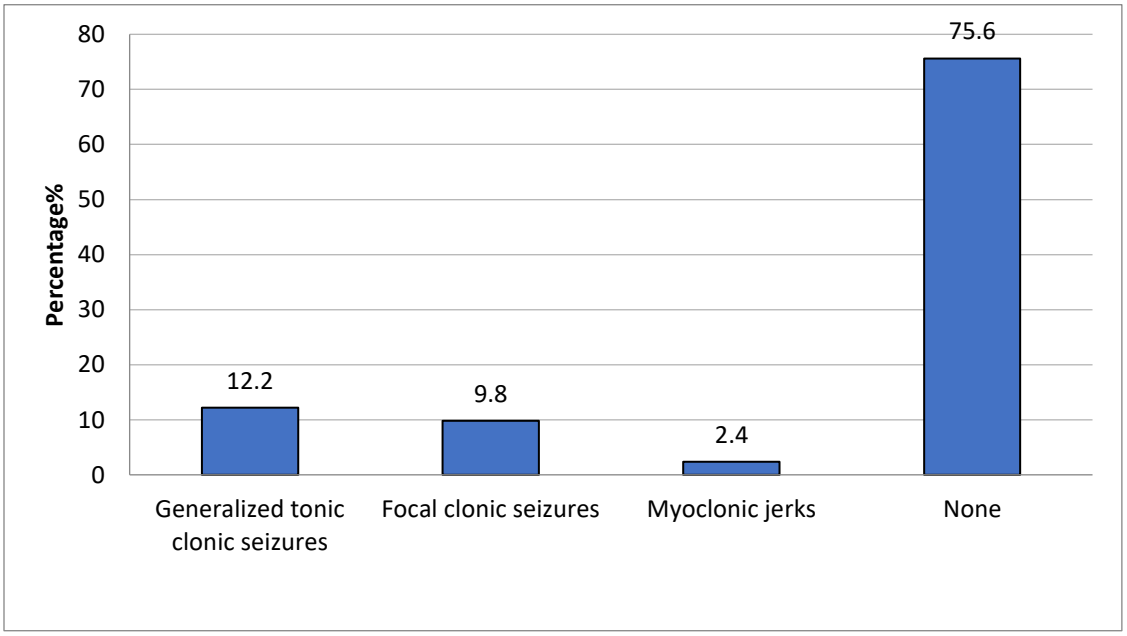
OTHER TYPE OF SEIZURES

Ten (24.4%) children with epileptic spasms had additional types of seizures including generalized tonic clonic in 5 (12.2%), and focal clonic in 4 (9.8%). One child had myoclonic seizures. In majority (75.6%), epileptic spasms were the only type of seizures. (Table 8)

Table 8: Other types of seizures.

Other types of seizures	No. of cases	Percentage (%)
Generalized tonic clonic seizures	5	12.2
Focal clonic seizures	4	9.8
Myoclonic jerks	1	2.4
None	31	75.6
Total	41	100

Figure 8: Other types of seizures.



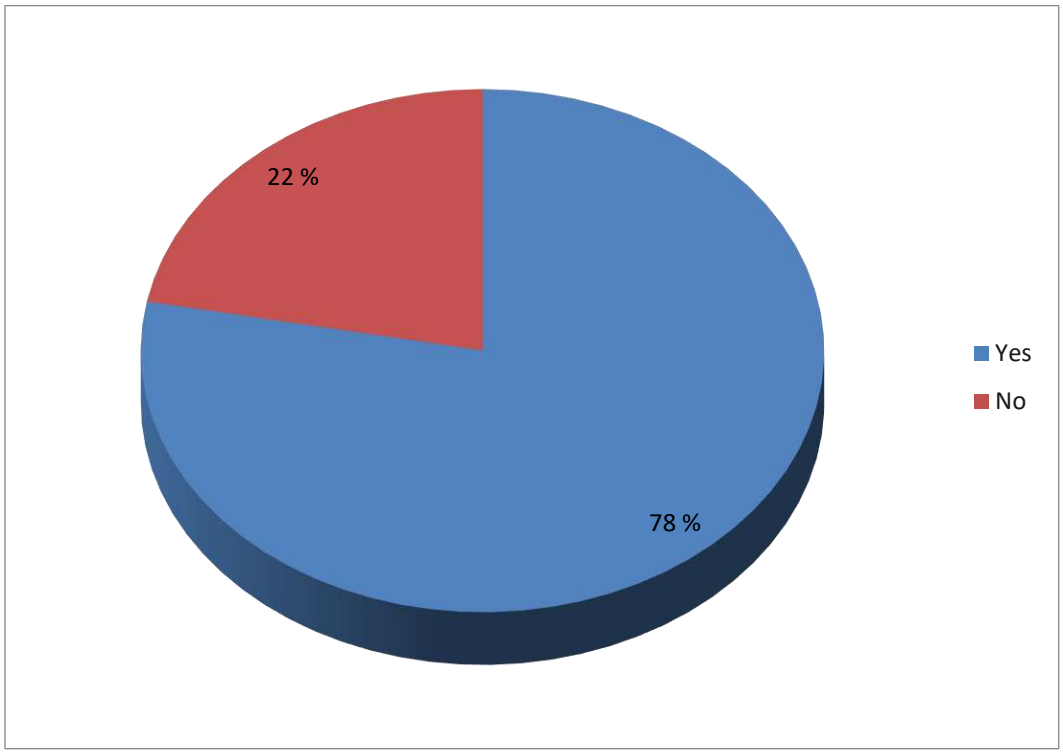
HOME- VIDEO RECORDED BY PARENTS

In majority of the children, 32 (78%) presenting with epileptic spasms, parents had recorded the home video of the spasms and was brought for review. (Table 9, Figure 9)

Table 9: Home videos recorded by parents.

Video recorded	No. of cases	Percentage (%)
Yes	32	78
No	9	22
Total	41	100

Figure 9: Home videos recorded by parents.



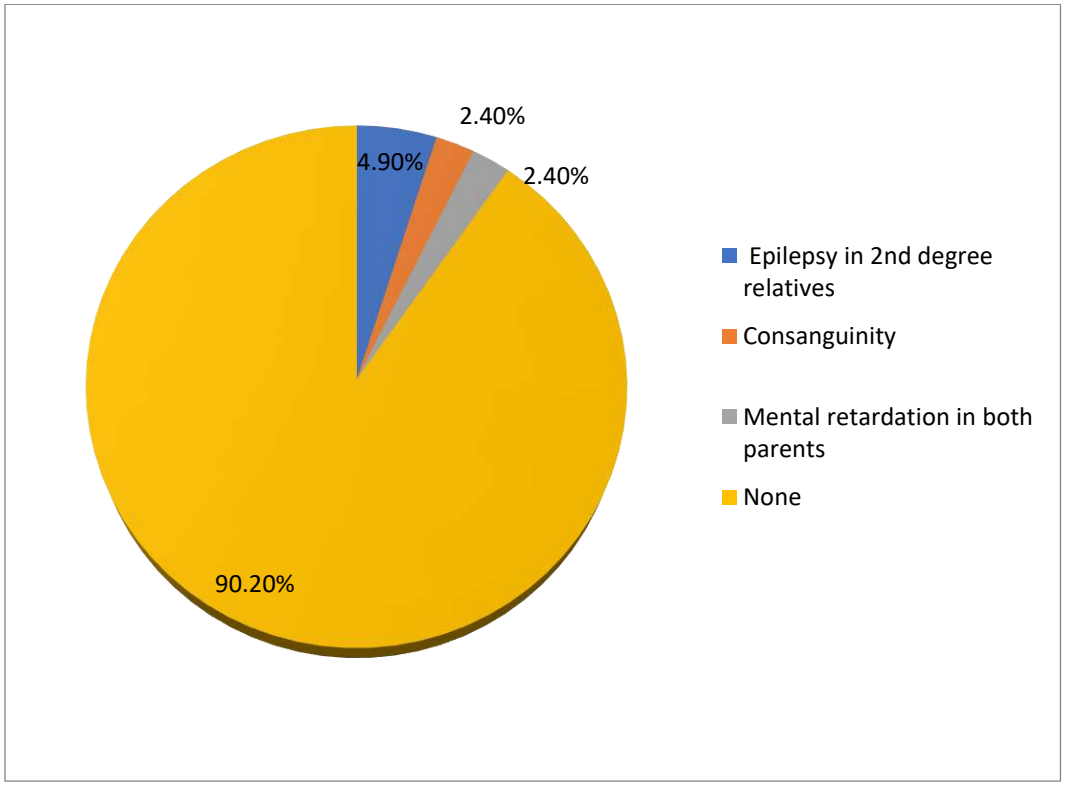
FAMILY HISTORY

In majority of cases 37(90.2%), there was no family history of epileptic spasms or epilepsy. In 2 patients (4.9%) history of epilepsy in 2nd degree relatives was noted. One case had mental retardation in both parents. (Table 10).

Table 10: Family history of children with epileptic spasms.

Family history	No. of cases	Percentage (%)
Epilepsy in 2nd degree relatives	2	4.9
Consanguinity	1	2.4
Mental retardation in both parents	1	2.4
None	37	90.2
Total	41	100

Figure 10: Family history of children with epileptic spasms.



BIRTH HISTORY

Majority (65.9%) children were born via LSCS, 14 cases (34.1%) were born by vaginal delivery (Table 11). Twenty-seven (65.9%) were born full-term, and 34.1% preterm.

Table 11: Mode of delivery of children with epileptic spasms.

Birth history	No. of cases	Percentage (%)
LSCS	27	65.9
NVD	14	34.1
Total	41	100

Figure 11: Mode of delivery of children with epileptic spasms.

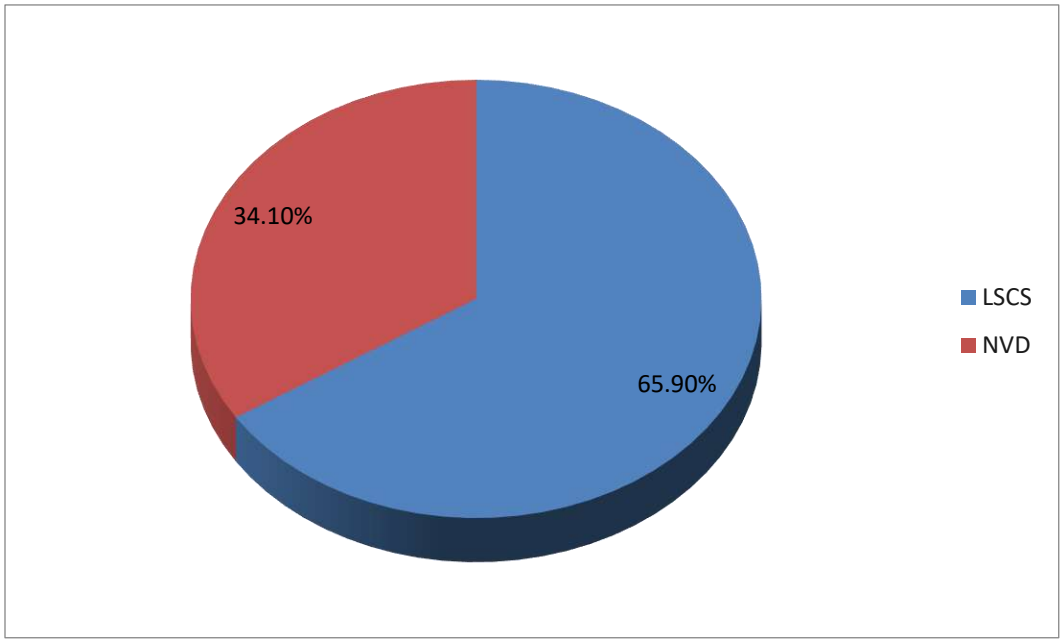
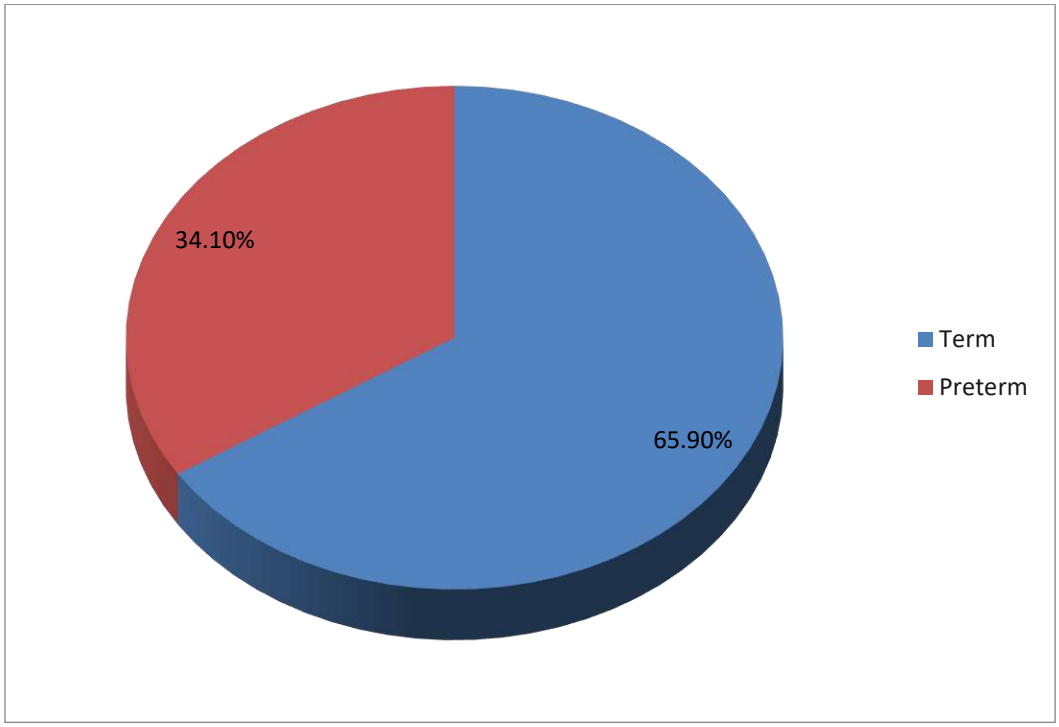


Table 12: Gestational age at birth of children with epileptic spasms.

Gestation	No. of cases	Percentage (%)
Term	27	65.9
Preterm	14	34.1
Total	41	100.0

Figure 12: Gestational age at birth of children with epileptic spasms.



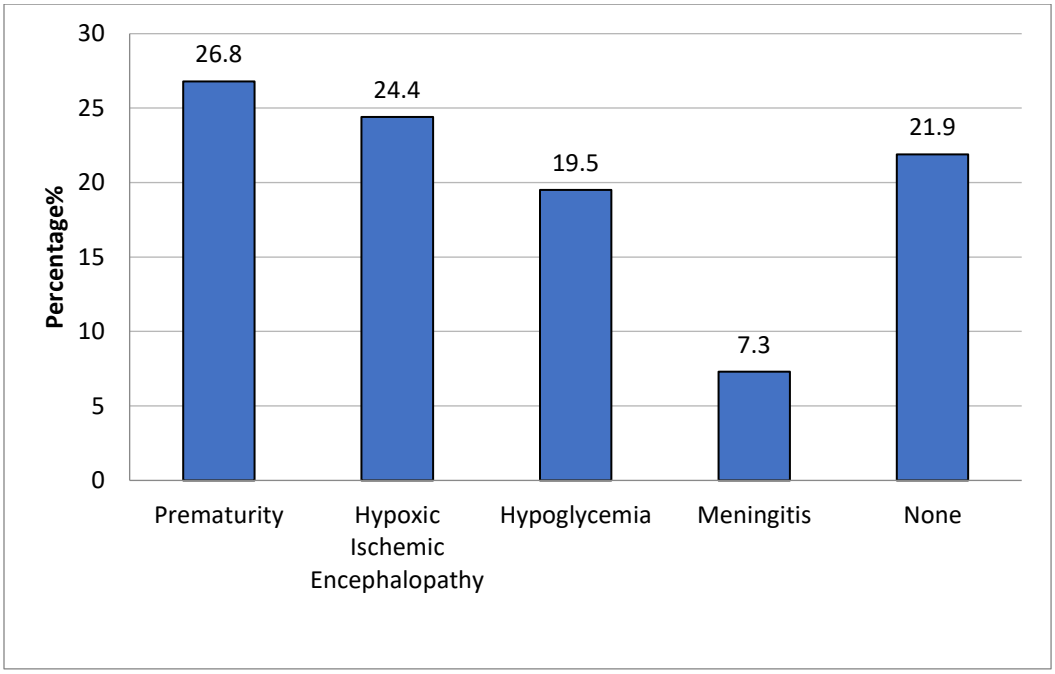
PERINATAL ILLNESSES

Among 41 children evaluated, 26.8% (11 cases) had prematurity, 10 (24.4%) children had Hypoxic ischemic encephalopathy, 8 (19.5%) had hypoglycemia, 3 (7.3%) had meningitis, 9 cases (21.9%) had no perinatal illnesses. (Table 13)

Table 13: Perinatal illnesses.

Perinatal illnesses	No. of cases	Percentage (%)
Prematurity	11	26.8
Hypoxic Ischemic Encephalopathy	10	24.4
Hypoglycemia	8	19.5
Meningitis	3	7.3
None	9	21.9
Total	41	100

Figure 13: Perinatal illnesses.



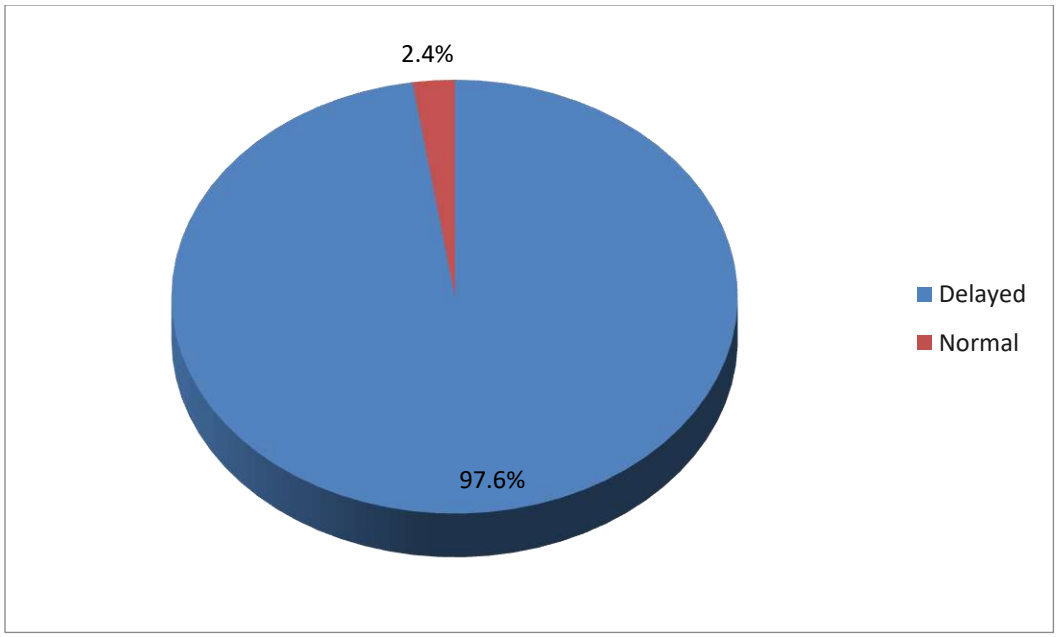
DEVELOPMENT

Only 1 case had normal development out of the 41 children, rest all had developmental delay prior to the onset of epileptic spasms.

Table 14: Developmental status prior to onset of epileptic spasms.

DEVELOPMENT	No. of cases	Percentage (%)
Delayed	40	97.6
Normal	1	2.4
Total	41	100

Figure 14: Developmental status prior to onset of epileptic spasms.



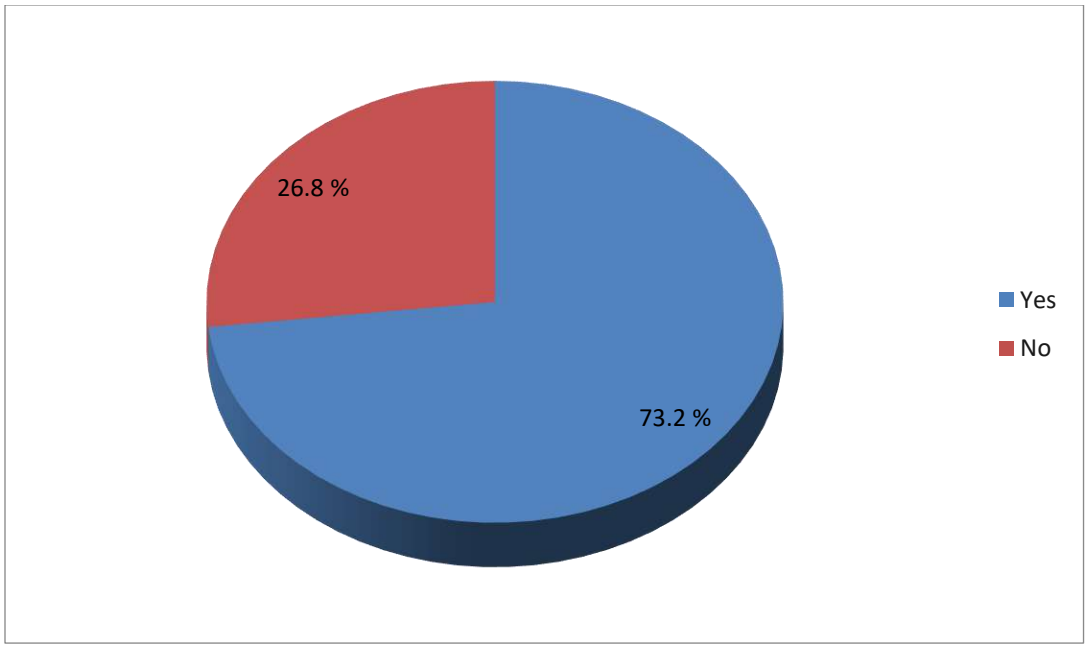
DEVELOPMENTAL SLOWING OR REGRESSION SINCE ONSET OF SPASMS

Thirty cases (73.2%) had developmental slowing or regression since the onset of spasms and 11 cases had no regression or slowing.

Table 15: Developmental slowing or regression since the onset of spasms.

DEVELOPMENTAL SLOWING OR REGRESSION SINCE ONSET OF SPASMS	No. of cases	Percentage (%)
Yes	30	73.2
No	11	26.8
Total	41	100

Figure 15: Developmental slowing or regression since onset of spasms.



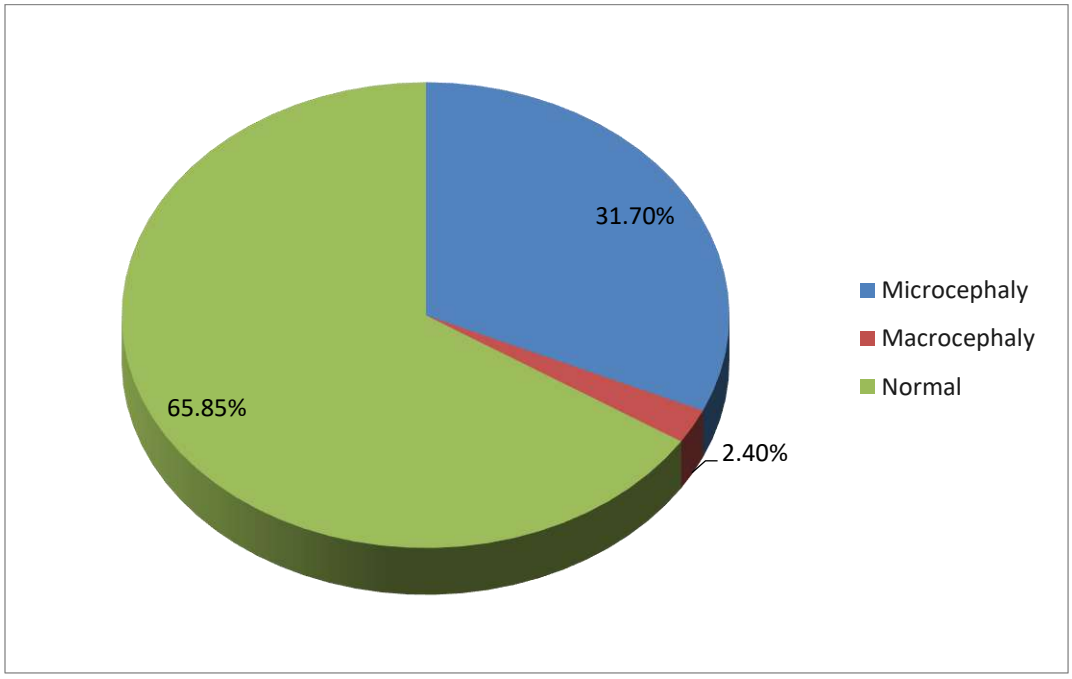
GENERAL PHYSICAL EXAMINATION

Out of the 41 patients, microcephaly was noted in 13 cases (31.7%), 1 patient had macrocephaly (2.4%) and rest of the 27 patients (65.85%) had normal head circumference. (Table 16)

Table 16: Head Circumference of children with epileptic spasms at the time of presentation.

Head Circumference	No. of cases	Percentage (%)
Microcephaly	13	31.7
Macrocephaly	1	2.4
Normal	27	65.85

Figure 16: Head Circumference of children with epileptic spasms at the time of presentation.



Only 1 patient had dysmorphic features on examination. This child had Down syndrome. No patients had neurocutaneous signs on examination.

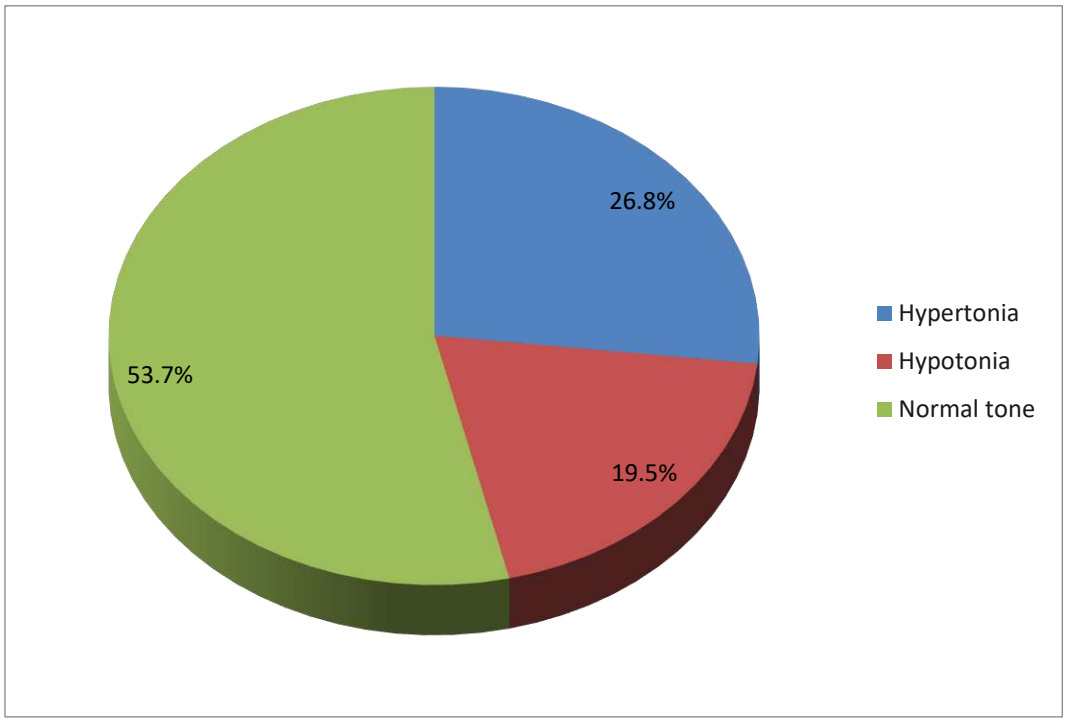
NEUROLOGICAL EXAMINATION

Eleven patients (26.8%) had hypertonia on examination and 8 (19.5%) had hypotonia on neurological examination.

Table 17: Findings on neurological examination in children with epileptic spasms.

Neurological examination	No. of cases	Percentage (%)
Hypertonia	11	26.8
Hypotonia	8	19.5
Normal tone	22	53.7
Total	41	100

Figure 17: Findings on neurological examination in children with epileptic spasms.



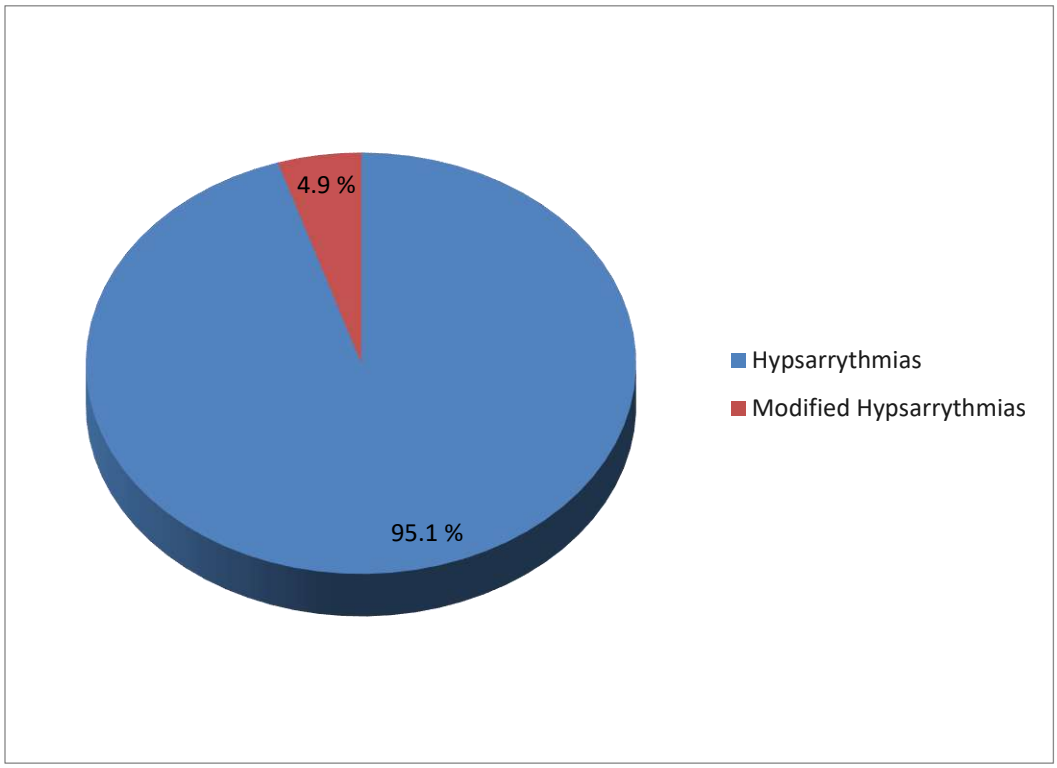
Electroencephalography (EEG)

All patients underwent EEG and had hypsarrhythmia; 39 patients (95.1%) had hypsarrhythmia and 2 (4.9%) had modified hypsarrhythmia. (Table 18)

Table 18: EEG Findings in children with epileptic spasms.

EEG	No. of cases	Percentage (%)
Hypsarrythmia	39	95.1
Modified Hypsarrythmia	2	4.9
Total	41	100

Figure 18: EEG Findings in children with epileptic spasms.



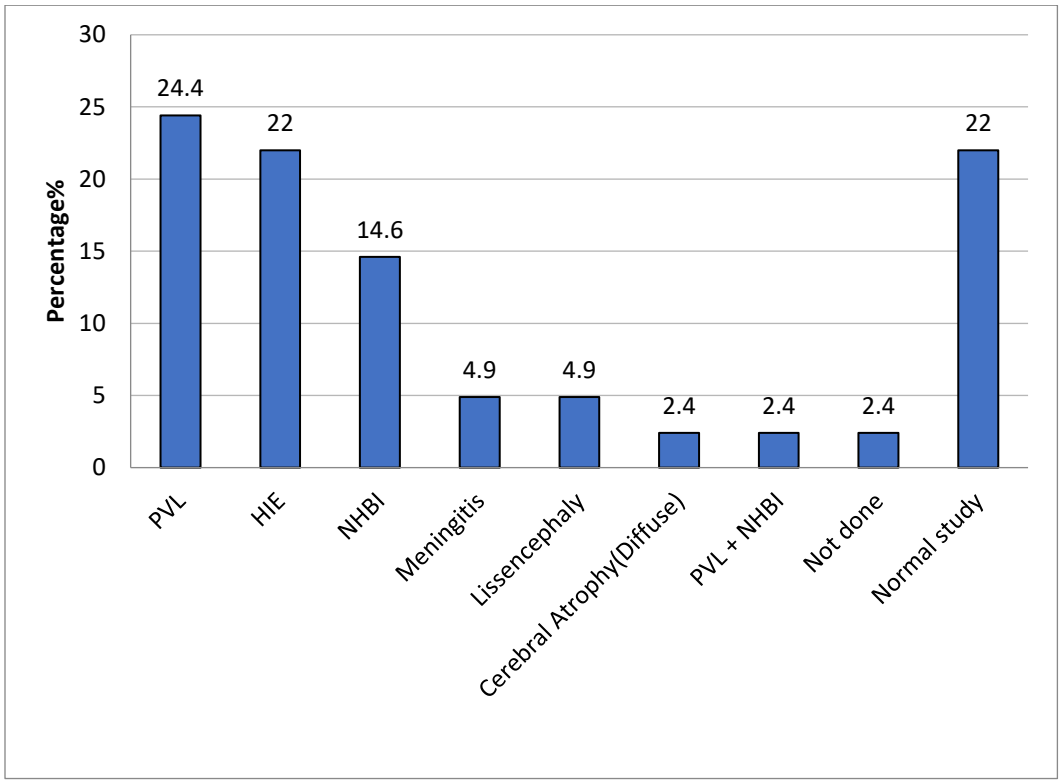
Brain MRI

40 out of 41 patients underwent MRI brain. In 1 patient MRI could not be done because of parents reluctance. Overall 31 (75.6%) showed abnormal neuroimaging findings. As depicted in Table 19., Ten children (24.4%) had brain MRI findings suggesting periventricular leukomalacia(PVL), and 9 patients (22%) had findings suggestive of hypoxic ischemic injury . Six children had findings consistent with neonatal hypoglycemic brain injury (NHBI). Lissencephaly was diagnosed in 2 cases (4.9%), and 2 had neonatal meningitis. One child had findings of both periventricular leukomalacia and neonatal hypoglycemic brain injury. In 9 children (22%), brain MRI was normal.

Table 19: MRI Findings in children with epileptic spasms.

MRI Findings	**No. of cases**	**Percentage (%)**
Periventricular Leukomalacia (PVL)	10	24.4
Hypoxic Ischemic Encephalopathy (HIE)	9	22.0
Neonatal hypoglycemic brain injury (NHBI)	6	14.6
Meningitis	2	4.9
Lissencephaly	2	4.9
Diffuse Cerebral Atrophy	1	2.4
PVL + NHBI	1	2.4
Not done	1	2.4
Normal study	9	22
Total	41	100

Figure 19: MRI Findings in children with epileptic spasms.



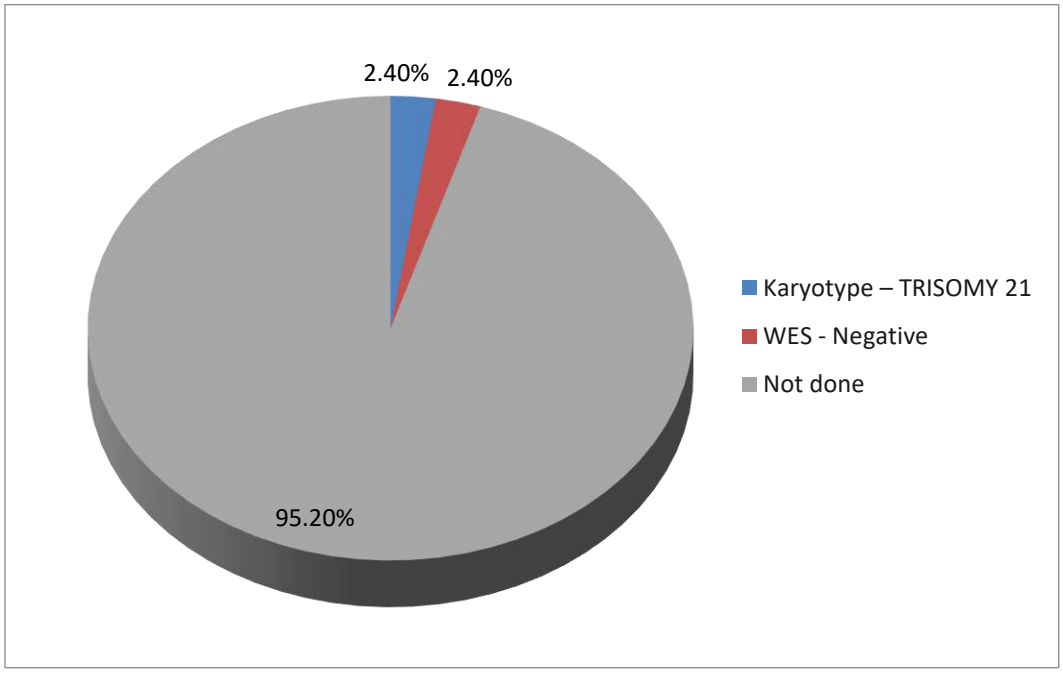
GENETIC STUDIES

Patient with down syndrome had trisomy 21 on karyotyping. One patient underwent whole exome sequencing but showed no genetic variant (Table 20).

Table 20: Genetic studies.

GENETIC STUDIES	No. of cases	Percentage (%)
Karyotype – TRISOMY 21	1	2.4
WES –Negative	1	2.4
Not done	39	95.2
Total	41	100

Figure 20: Genetic studies.



FINAL ETIOLOGICAL DIAGNOSIS

Etiological diagnosis of the children presenting with epileptic spasms is given in table 21. Hypoxic Ischemic Encepahlopathy (HIE) accounted for 19 (46.3%) cases. Neonatal hypoglycemic brain injury (NHBI)in 7 cases (17.1%), Lissencephaly in 2 , Meningitis in 2, Nutritional Vitamin B12 deficiency in 1 , Downs syndrome in 1 case . In 9 cases (21.9%), no obvious etiology was found.

Table 21: Etiological diagnosis of patients presenting with epileptic spasms.

ETIOLOGICAL DIAGNOSIS	No. of cases	Percentage (%)
STRUCTURAL – ACQUIRED	**29**	**70.7**
HIE	19	46.3
NHBI	7	17.1
Meningitis	2	4.9
Nutritional Vitamin B12 Deficiency	1	2.4
STRUCTURAL- GENETIC	**2**	**4.9**
Lissencephaly	2	4.9
GENETIC	**1**	**2.4**
Downs syndrome	1	2.4
IDIOPATHIC / UNKNOWN	**9**	**21.9**
Total	**41**	**100.0**

Figure 21: Etiological diagnosis of patients presenting with epileptic spasms.

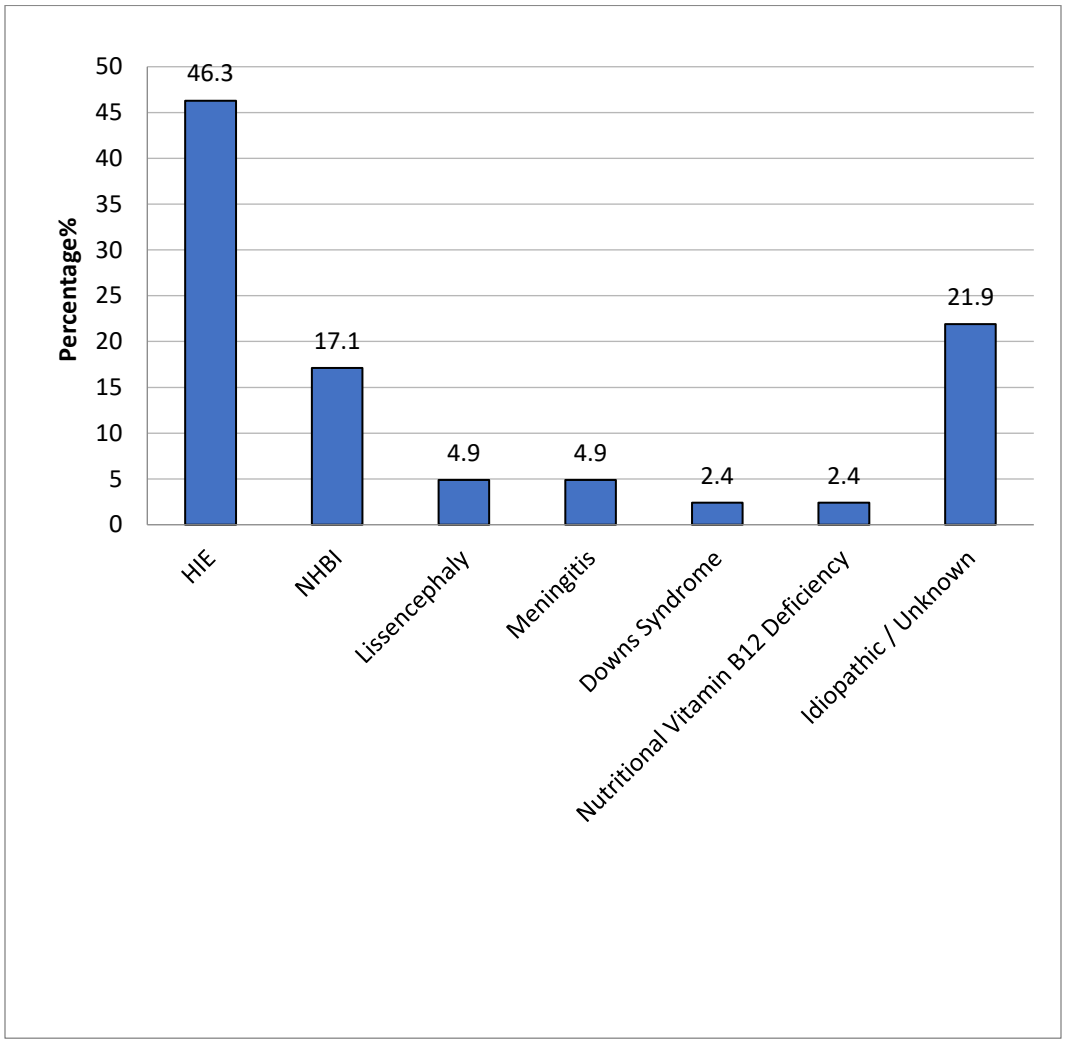
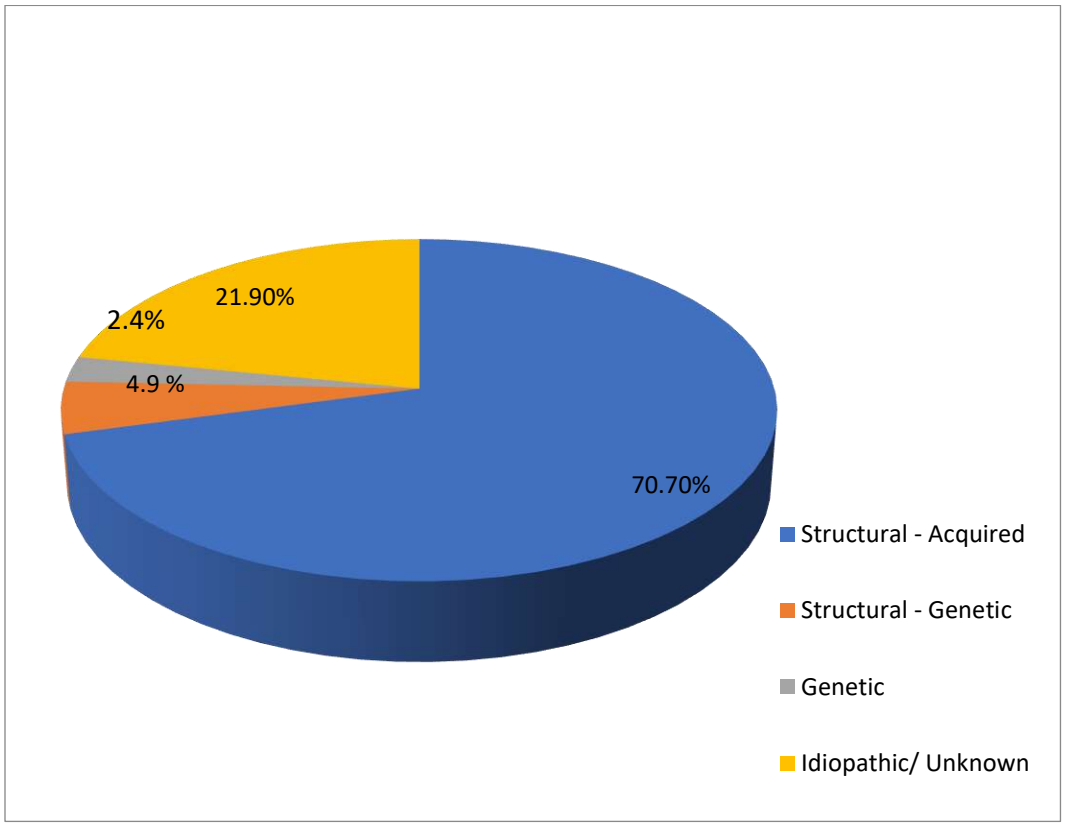


Figure 22: Final diagnosis of patients presenting with epileptic spasms.



DISCUSSION

Epileptic spasms are a devastating form of seizures and epilepsy in children and are often associated with poor long-term seizure control and neurodevelopmental outcomes.[10] Epileptic spasms are in most cases the result of underlying serious neuropathological substrate, often acquired in the perinatal period. While hypoxic ischemic brain damage continues to dominate the clinical picture, the spectrum of disorders associated with epileptic spasms has undergone significant change over time, attributed to large extent to advances in neuroimaging and genetics, and improved perinatal care.[21]

There are many studies from the developed countries, but only fewer from Indian subcontinent, focusing on the etiology and clinical profile of epileptic spasms. This study was intended to find the clinical and etiological characteristics of epileptic spasms in the current times in the setting of developing countries like India, where preventable risk factors such as perinatal hypoxia and hypoglycemic brain injury have been identified as the most common causes of epileptic spasms.[18,20,21,40,41] It is hoped that identification of these factors will be helpful in devising and rationalizing better diagnostic, therapeutic and preventive interventions.

During the 18-month study period, between March 2021 to September 2022, we recruited 41 patients older than 1 month of age with the diagnosis of new onset epileptic spasms. Out of 41, 40 patients presented in pediatric neurology out-patient services, and one was recruited from in-patient services. This can be explained by the fact that epileptic spasms appear less alarming to parents, and also not infrequently, are misrecognized as simple startle response, abdominal colic, or even not recognized at all unless specifically asked by the physician.

In our study, children presented between age group of 4 months to 3.5 years of age (Table 1). Majority of the children (80%) were under 2 years of age with 44% being in the age group of 6 months to 12 months, at the time presentation to the hospital. The age of onset of spasms was

between 6 months to 12 months in 21 (51%) children, followed by 10 (24%) children having spasms onset before 6 months of age. Four (9.8%) children were between 13 months to 24 months of age, while 6 (14.6%) children were between 2 years to 3.5 years age. Mean age of onset of epileptic spasms was 12 months (Table 3). In comparison with other studies where mean age of onset was found to be between 5.5- 8 months.[20,40,41]In a study by Sehgal et al. mean age of onset of spasms was found to be 5.5 months.[20] In another study , by Gupta et al. mean age of onset was found to be 7.5 months.[40] Mean age of onset was found to be 8.12 months in the study by Nawaz et al.[41]ILAE has recently changed the nomenclature of Infantile spasms to epileptic spasms to include older children with epileptic spasms because epileptic spasms are not restricted to infancy but can be seen in older children. In our study, at least 1/4th (24%) were older than 2 years of age at the time of onset of epileptic spasms explaining the higher mean age of onset and also corroborating the term epileptic spasms instead of Infantile spasms.

In a study by Kalra et al., the median age of onset of spasms was noted to be 3 months and age of presentation was 10 months,[38] suggesting later recognition and presentation of children with epileptic spasms . In our study, the mean age of presentation was 16 months, in comparison with the age of onset of spasms which was 12 months. Similar to other Indian studies, lag time found in our study was 4 months but it was longer as compared to that noted in developed nations. In a retrospective study of western France, the mean time from appearance of first symptom to first visit to hospital was 4 weeks.[45] In another study from western world, the median time from the onset of infantile spasms to first visit with an effective provider was 24.5 days.[46] Delay in diagnosis can be justified by the nature of spasms, which can be so subtle that it is often not recognized by the parents and can be misinterpreted as startle response, or abdominal colic.[1] In addition, it was also noted in our study that most of the children presenting with epileptic spasms were already on some

antiepileptics prescribed by general practitioners, who probably had misdiagnosed epileptic spasms with other seizure types due to lack of knowledge of epileptic spasms, leading to delayed diagnosis.

Male patients have been affected more frequently than females in previous studies. [18,19,36,38,41] In a study by Kaushik et. al. out of 148 patients enrolled, 120 (81.1%) were boys.[18] In the study by Singhi et al. 67.9% children were males.[19] In another study by Kulsoom et al. male preponderance was noted with male to female ratio of 2:1.[36] We also noted the male predominance in our study with male to female ratio of 4.8:1 (Table 2). But it was quite marked as compared to previous studies. To some extent it can be explained on the basis of gender bias in seeking medical attention in our country.

Epileptic spasms are classified as flexor, extensor or mixed flexor-extensor, flexor types being the most frequent types of epileptic spasms.[28,29] Gupta et. al in her study reported flexor spasms in 97.6% cases.[40] In another study of 39 children, majority (87.5%) of children had flexor spasms.[41] Kaushik et al. found flexor spasms in 76% cases, extensor spasms in 6.2% and mixed in 17.6%.[18] In our study too, majority of the patients had flexor spasms (83%), followed by extensor spasms in 12% patients and mixed type of spasms in 5% patients (Table 4).

Characteristically, epileptic spasms occur in clusters with variable number of clusters per day and number of spasms per cluster. All the 41 children had clustering of spasms with an average of 6 spasms per cluster with each cluster lasting for around 1 minute to 5 minutes with a mean of 3 minutes (Table 5). A mean of 10 clusters per day, with each cluster having 5 spasms was noted in a study by Kaushik et. al.[18] In another study**,** average spasms per cluster were found to be 6.33 (range 1 to 20) and average clusters per day were 5.87 (1 to 20).[41] Gehlawat et al. in his study found , majority of patients had clusters with average of 5 (4 to 6) spasms per cluster.[42]

Epileptic spasms have a close relation with the circadian rhythm of sleep wake cycle with majority of spasms occurring on awakening. Occurrence of spasms on awakening was noted in our study in 82.9 % children while 9.8% children had spasms when drowsy and 7.3% children had spasms during sleep (Table 6). In the study by Khreisat, 96% cases of infantile spasms occurred on awakening from sleep.[27] In another study, association of spasms with sleep wake cycle was observed in only 52% cases.[40] Relationship of spasms with the sleep–wake cycle was found in 108 (72.9%) children by Kaushik and colleagues.[18]

We also studied other symptoms associated with epileptic spasms.[14] Overall, 95% children had these symptoms. Twenty-eight(68%) children were noted to have crying during/after each epileptic spasm. Eight (20%) children had laughing during the episodes and 7% had vomiting (Table 7). Associated behavior change was reported in the form of cry, squeal or irritability in 30.9% cases in a study by Singhi et al.[19] High percentage of associated symptoms found in our study could possibly be because , ours was a prospective study and we specifically looked for these symptoms in our patients.

Other seizure types may occur before or after the onset of infantile spasms*.* Khreisat et al. reported other types of seizures in 44% children, these were focal (16%), generalized tonic clonic (20%) and other types (8%).[27] Similarly, Singhi et al. found other types of seizures also accompanied epileptic spasms in 31 children (18.7%), these were focal (6%), generalized tonic clonic (8.5%) and other types (1.2%). In a study by Yamamoto et al. 36 % children with epileptic spasms had other types of seizures prior to the onset of infantile spasms.[47] Our study was also keeping in with these findings. In our study, 24% children were found to have other seizure types. Among which 5 patients had tonic clonic seizures (12.2%), 4 had focal clonic seizures (9.8%) and 1 patient had myoclonic jerks (Table 8).

An interesting observation regarding epileptic spasms in our study was that in majority of the cases with epileptic spasms, parents had the video recording of the spasms and brought it for review in the clinic (Table 9). It was confirmatory of the diagnosis in all the patients. Home videos have been found to be very helpful in the diagnosis of seizure and seizure types as well as its differentiation from non-epileptic spells.[48-50] In a prospective study assessing the effectiveness of telemedicine among 78 children between 4 months and 7 years of age with West syndrome. Compared to face-to-face consultation, teleconsultation (which included home video recordings) had more sensitivity and specificity in diagnosis.[51]

In our study, no patient had family history of epileptic spasms. There was history of epilepsy in 2nd degree relatives in 2 patients. History of mental retardation in both parents was present in 1 case. History of consanguinity was present in 1 case (Table 10). All these findings point towards possibility of genetic factors in the etiology of epileptic spasms, [52-55] but detailed metabolic or genetic investigations were not done because of financial constraints. A genetic predisposition to cause Infantile spasms was noticed by Dulac et al. and by Hemminki et al., on the basis of the observation that the chance of having Infantile spasms was increased in families in which other members were affected by epileptic seizures. A genetic predisposition in cases of Infantile spasms was also confirmed by reports of Infantile spasms in twins.[52,53] Pavone et al. & Coppola et al. have described the occurrence of Infantile spasms in a set of monozygotic twins, the epileptic spasms appeared on the same day, within hours in both the twins.[54,55]

Most of the studies have recognized developmental delay predating the onset of epileptic spasms. Developmental regression with disappearance of social smile, loss of visual attention or autistic withdrawal were observed in 70% of the children with the onset of spasms by Kramer et al.[56] Developmental delay prior to onset of spasms

was found to be 93% by Kaushik et al, 88% by Chandra et al, and 92% by Iype et al.[18,57,58] In Another study from western India, developmental delay was found in 31 (94%) out of 33 children.[41] We also found high prevalence of developmental delay at presentation noted in 40 (97.5%) children in our cohort (Table 14). Further developmental regression or slowing, a well-known phenomenon with epileptic spasms,[10] occurred in 30 children in our study(Table15). While most of the developmental delay is caused by underlying neuropathology epileptic spasms per say can cause psychomotor retardation and regression through mechanisms that are not well defined.

Since, epileptic spasms occur in setting of pre- or perinatal brain damage, neurological abnormalities are common on examination. In our study we noted microcephaly in 13 (32%) patients and 1 patient had macrocephaly (Table 16). Eleven cases had spasticity and 8 hypotonia on neurological examination (Table 17). One patient had dysmorphic features, and no patient had neurocutaneous markers. Nineteen (46%) cases had a diagnosis of cerebral palsy. These findings are consistent with the previous studies. In the study by Kalra et al. microcephaly was noted in 43 cases (48.3%).[38] Gehlawat et al. also found microcephaly in 16 cases(53.3%).[42] It suggests the involvement of brain parenchyma even before the onset of epileptic spasms.[19,38]In previous studies , cerebral palsy was found in 67% & 60% cases by Gupta et al. & Khreisat respectively.[27,40] In another Indian study, 77 children(46.6%) out of 165 had cerebral palsy of different types, most common being spastic quadriplegia and microcephaly was seen in 72.7% cases.[19]

As per inclusion criteria, all our patients underwent EEG recording, and all showed hypsarrhythmia including 2 with modified hypsarrhythmia (Table 18). Similar to our study, hypsarrhythmia was the most common EEG finding (in 69% cases) followed by modified hypsarrhythmia (31% cases) in a study by Kulsoom et al.[36] In another study, hypsarrhythmia was seen in 44% children with other patterns(focal discharges, spike and

slow wave abnormality, burst suppression pattern) in 49% cases and normal EEG in 7% patients.[19]

In our study, brain MRI was done in 40 children. Neuroimaging could not be done in 1 child with cerebral palsy related to prematurity. Among 40 patients, 10 patients (24.4%) had periventricular leukomalacia (PVL), 9 (22%) had changes of hypoxic-ischemic brain damage. In 6 (14.6%) patients brain MRI showed changes of neonatal hypoglycemic brain injury. Two cases (4.9%) had Lissencephaly. In 2 patients brain showed structural changes secondary to meningitis. One child had diffuse cerebral atrophy. One child showed findings of both Periventricular leukomalacia and neonatal hypoglycemic brain injury. Brain MRI was normal in 9 patients (22%) (Table 19). All these brain changes on MRI reflect underlying neuropathology. Aydinli et al. in a study on neuroradiological aspects of West Syndrome conducted in 143 patients reported, out of 78 children who underwent MRI, only 14 had normal scans. Cerebral malformations, cerebral atrophy and delayed myelination were the most common findings.[59] In a recent Indian study by Gupta et al, out of the 53 patients who underwent MRI, most common abnormality found on MRI was periventricular leucomalacia in 11 patients (20.7%), followed by hypoxic ischemic encephalopathy in 9 patients (17%). Neonatal hypoglycemic brain injury was found in 4 cases (7.5%). In 7 patients (13.2%) MRI were reported normal. In patients who underwent both neuroimaging methods (CT & MRI), MRI was found to be more informative.[40] In another study by Kulsoom & colleagues, MRI was carried out in all 36 patients; it was normal in 64% and abnormal in 36%. Most common radiological findings were vascular events (ischemia/hemorrhage in 46%) followed by congenital brain malformations (23%).[36] Some of the results in our study could have been influenced by small sample size, resulting in relative scarcity of tuberous sclerosis and brain malformations. On the other hand, in addition to hypoxic ischemic brain damage, we have

preponderance of neonatal hypoglycemic brain injury, which is particularly common in our set up.[21]

Out of the 41 children studied, 14(34%) were born preterm and 27(66%) were term deliveries (Table 12). Prematurity have been described as a common risk factor for epileptic spasms and West syndrome in various studies. In a study by Ibrahim, history of prematurity was present in 14 (25%) cases.[60] In other studies by Kaushik et al. & Gehlawat et al, epileptic spasms were attributed to prematurity in 3(2.4%) cases & 8(26%) cases respectively.[18,42] Most (66%) of the children were born by cesarean section and 34% were born by vaginal delivery in our study (Table11).

We used ILAE 2017 classification for dividing our patients into different etiological diagnosis groups.[21] Most of our patients belonged to Structural – acquired group, i.e. 70.7% patients (Table 21). In structural-acquired group, Hypoxic ischemic encephalopathy (46.3%) was the commonest etiology followed by NHBI (17.1%), 2 patients had meningitis and in 1 patient preceding vitamin B12 deficiency(spasms occurred during recovery phase) was considered as the etiological factor. Two patients with lissencephaly were grouped under structural – genetic group. 1 patient with Downs syndrome was classified under Genetic group. In 9 patients (21.9%), no etiology was identified, they were grouped under Unknown/ Idiopathic. Similar to our study , in the recent study by Surana et al, patients were grouped into: Structural, Genetic and Unknown. Etiology was ascertained in 94/113 (83.1%) with neonatal hypoglycemic brain injury (NHBI) being the most common 40/113 (36%). A genetic etiology was identified in 17.[21]

Perinatal brain injury has been recognized as the most common cause of infantile spasms worldwide. In studies by Wirell & Osborne, prenatal causes were found most common, accounting for 57.8% and 49.6% of known etiologies respectively. Prenatal causes included structural malformations, chromosomal, metabolic disorders and other genetic etiologies. In both the studies, perinatal etiologies were causal in

approximately one fourth of known causes, with the most common etiologies being hypoxic-ischemic encephalopathy and brain injury of the preterm infant.[6,13] In another study, by Cowan et al. prenatal factors including selected syndromes (eg, Aicardi syndrome, Down syndrome, etc) and inherited disorders (eg, tuberous sclerosis) accounted for as many as one third of cases.[61] In the study of 180 patients by Ohtahara et al. prenatal cause was the most frequent diagnosis (77 cases, 42.8%), followed by perinatal (25 cases, 13.9%) and postnatal factors (12 cases, 6.7%); 48 cases (26.7%) were of uncertain etiology; eighteen cases (10.0%) were idiopathic. Prenatal factors of West Syndrome included tuberous sclerosis (23), chromosome abnormalities (10), cerebral dysgenesis (10), porencephaly (7), hydrocephalus (5), Aicardi syndrome (3), Aicardi syndrome associated with chromosome abnormality (1), and other causes (18). [62]

In most of the Indian studies, perinatal causes have been identified as the major risk factor for epileptic spasms. Perinatal asphyxia and neonatal hypoglycemic brain injury account for majority of the cases of epileptic spasms, in India. Sehgal et al. in her study reported, perinatal asphyxia (which probably also included unrecognised cases of neonatal hypoglycemia) in 43 out of 95 (45.2%), neonatal sepsis/meningitis in 29/95 (29.5%) and neonatal jaundice requiring phototherapy or exchange transfusion in 8/95 (8.9%).[20] In another study from North India, the perinatal cause accounted for majority of the cases with perinatal asphyxia (40.9%) being the commonest, followed by neonatal hypoglycemia (14.8%) and neonatal meningitis (9.8%). Prenatal causes were found in 7.8% cases and postnatal meningitis accounted for 6% of the cases.[40]

Similar to other Indian studies, our study has also identified, perinatal illnesses as the most common etiology, prematurity with PVHI/IVH resulting in Periventricular Leukomalacia being the most common cause accounting for 11(26.8%) cases of epileptic spasms followed by HIE/ perinatal asphyxia which was found in10(25%) cases.

Neonatal hypoglycemic brain injury for 8 (19.5%) cases. Meningitis occurred in 3(7.3%) cases. Nine (21.9%) cases had no identified perinatal illnesses (Table 13).

Apart from perinatal asphyxia, neonatal hypoglycemic brain injury has been found to be commonest perinatal cause leading to epileptic spasms in recent Indian studies. Neonatal hypoglycemic brain injury (40/113, 35.3%) was the most common acquired cause of epileptic spasms in the study by Surana et al.[21] In another Indian study , NHBI was found to be 2nd commonest cause after perinatal asphyxia , accounting for 14.8% cases by Gupta et al.[40] The higher incidence of neonatal hypoglycemia in developing countries has been found due to multiple factors including, but not limited to high prevalence of low birth weight , suboptimal neonatal care, excessive emphasis on exclusive breast feeding and reluctance to use of alternative feeds, and lack of support for mothers to help establish lactation.[63,64]

Owing to advanced genetic testing, genetic etiology of epileptic spasms is increasingly being recognized now. In a recent North Indian study, 11 patients (9.7%) had a mutation identified on genetic evaluation. Three patients (2 were dysmorphic) had microdeletions on array aCGH. Eight had point mutations on WES in CYFIP2, GRIN1, PRUNE, SCN2A, SIN3A, STXBP1 (two patients) and TUBB2A genes. There were 6 patients in the structural-genetic group, including 5 patients with Tuberous sclerosis & 1 with lissencephaly. Mutations in the TSC2 gene were detected in 4 of the 5 children diagnosed with Tuberous sclerosis.[21] We had a very small contribution by genetic factors in our cohort. Possibly because of small sample size (limited by COVID -19 pandemic), and lack of advanced genetic testing. We could perform next generation sequencing in only one child. We believe genetic testing of cases of unknown etiology would have yielded some positive results for mutations.

Limitations of the study: Our study period coincided with the second SARS CoV2 wave which affected patient recruitment, resulting in fewer than expected number of patients in our study. We also could not do genetic testing in most of our patients where no clear etiology was identified on neuroimaging or other investigations, largely due to financial constraints. Only one patient underwent next generation sequencing.

SUMMARY AND CONCLUSION

In conclusion, epileptic spasms are common epileptic seizures in infants and young children. While majority of the cases occurred under 2 years of age, significant number of children started having epileptic spasms after the age 2 years justifying the new ILAE term epileptic spams instead of infantile spasms. Boys were more frequently affected than girls. Flexor spasms were the most common type with clustering of spasms in all. Spasms mostly occurred on awakening. Other type of seizures occurred in one – fourth children. Developmental delay prior to onset of spasms was noted in all children except one. Most of them had developmental slowing or regression after onset of spasms. Microcephaly was the commonest associated finding. All patients had hypsarrhythmia on EEG. Brain MRI was the most helpful tool in determining the etiology of seizures. Periventricular leukomalacia, hypoxic ischemic brain injury, and neonatal hypoglycemic brain injury were the most common MRI findings. Etiologically, Two-third patients belonged to structural-acquired group of ILAE classification, followed by structural genetic group and genetic group. In a significant number of children, the etiology of epileptic spasms remained unknown.

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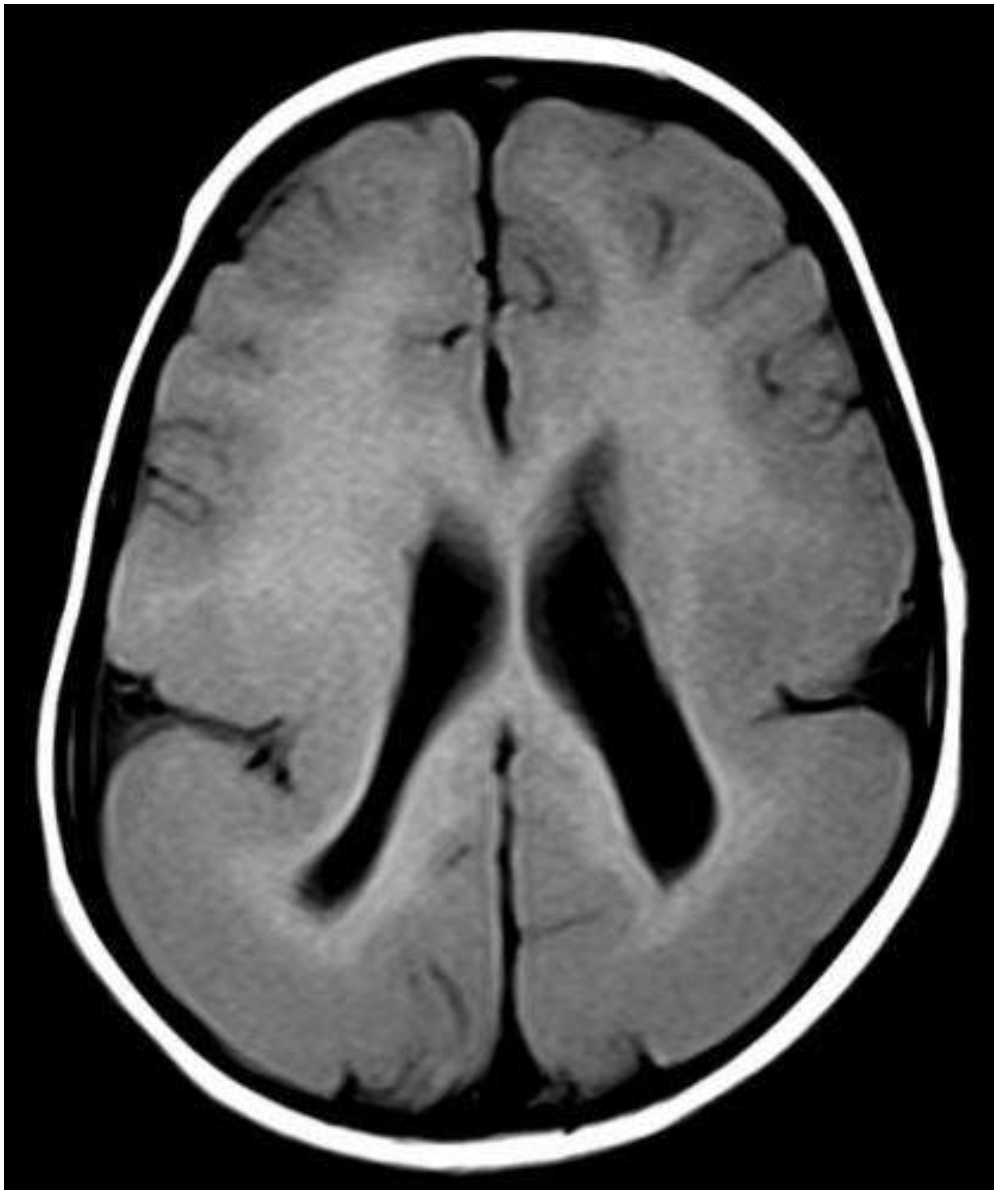
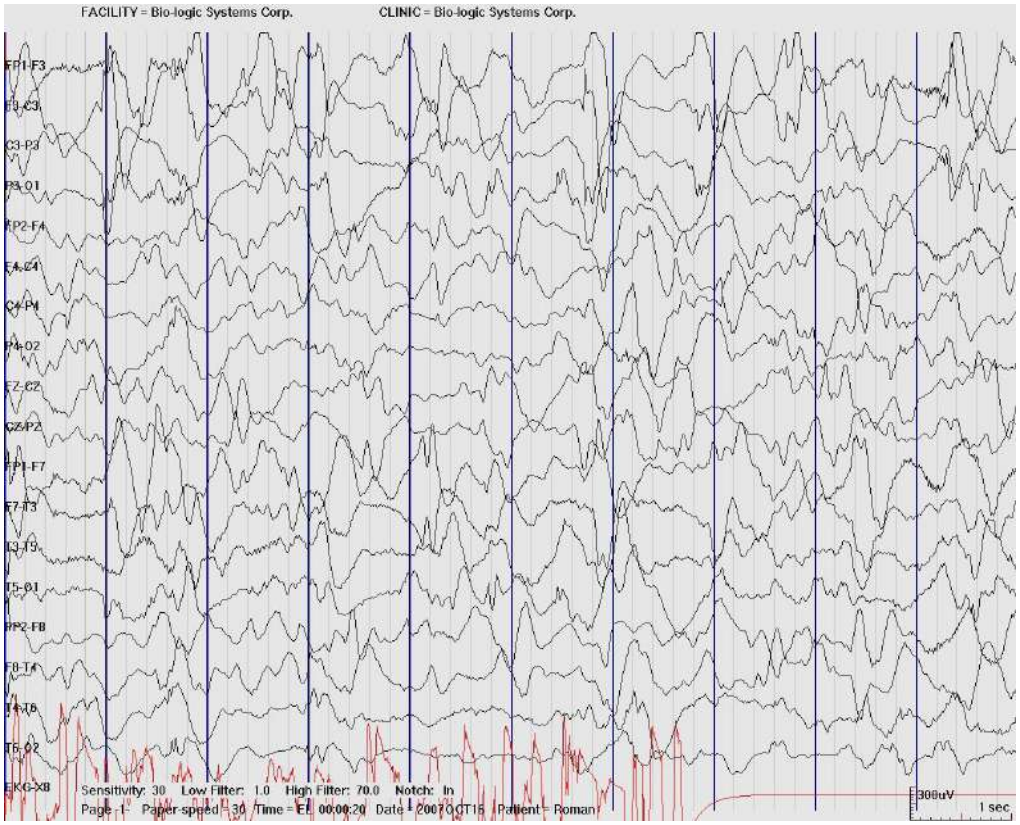


Picture 1: T1 weighted image of brain MRI showing lissencephaly. Figure-of-8 appearance is evident. Changes are more marked posteriorly than anteriorly.

Picture 2: FLAIR image of brain MRI showing bilateral occipital encephalomalacia and gliosis in a child with neonatal hypoglycemic brain injury (NHBI).

Picture 3: T2 weighted axial image of brain MRI showing ventricular dilatation with scalloped margins, and periventricular white matter hyperintensities suggestive of periventricular leukomalacia (PVL).

Picture 4: T2 weighted axial image of brain MRI showing thinning of corpus callosum, ventricular dilatation, and cerebral atrophy, especially marked in bilateral perisylvian region in an infant who suffered hypoxic ischemic encnephalopathy (HIE).



Picture 5: EEG showing large amplitude slow waves intermixed with multifocal spike, and electrodecremental response suggesting hypsarrhythmia.

S. NO	MRD NO.	INTIALS	AGE OF PRESENTATION (months)	SEX	DATE OF BIRTH	CHIEF COMPLAINTS	NARRATOR	AGE OF ONSET (in months)	TYPE OF SPASMS	CLUSTERING OF SPASMS	NO. OF SPASMS PER CLUSTER	DURATION OF CLUSTER (minutes)	TIME OF OCCURRENCE OF SPASMS	ASSOCIATED SYMPTOMS
1	1123620	AS	11	male	19-07-2020	Abnormal body movements since 5 months	Father	6	flexor	yes	5	2	On awakening	crying
2	1257090	A	30	male	08-02-2018	flexion spasms of neck since 1 & 1/2 yr of age	Father	12	flexor	yes	6	4	On awakening	laughing
3	1250329	A	7	male	13-07-2021	Abnormal body movements x 3 months	Mother	4	extensor	yes	6	2	When drowsy	none
4	1175116	A	34	male	11-02-2018	Twisting movements since birth , arching , Head jerks since 4-5 days	Grandmother	34	flexor	yes	8	5	On awakening	crying
5	1256454	A	7	male	08-11-2021	Abnormal body movements x 3 months	Father	4	flexor	yes	2	2	On awakening	laughing
6	1061850	AR	18	male	09-10-2019	Abnormal body movements in form of head jerks x 8 months	Mother	8	flexor	yes	8	2	On awakening	crying
7	1130256	AK	13	female	31-05-2020	Abnormal body movements x 5 months	Mother	10	flexor	yes	5	4	On awakening	none
8	1130901	BS	6	male	16-03-2021	Abnormal body movements x 10 days	Mother	6	flexor	yes	5	5	On awakening	crying
9	1146473	B	11	female	29-08-2020	Abnormal body movements x 2 months	Grandmother	9	flexor	yes	2	2	On awakening	crying
10	1147261	D	24	male	26-06-2019	Head jerks x 3 months	Mother	21	flexor	yes	4	1	On awakening	crying
11	1134164	FS	6	male	25-01-2021	Head jerks x 1 month	Mother	5	flexor	yes	10	4	On awakening	crying
12	1102467	FS	38	male	09-11-2018	Flexion spasms - head jerks x 6 months	Mother	32	flexor	yes	2	1	On awakening	crying
13	1267379	G	5	male	03-01-2022	Abnormal body movements x 10 days	Mother	5	flexor	yes	6	2	When asleep	crying
14	1266315	GK	7	female	08-11-2021	Head bangs x 7 days	Mother	7	flexor	yes	8	5	On awakening	crying
15	1293940	G	36	female	16-12-2018	Abnormal body movements since 8 months	Mother	28	flexor	yes	3	2	On awakening	crying
16	1164287	HD	9	male	25-11-2020	Abnormal body movements x 2 months	Mother	7	extensor	yes	10	5	On awakening	crying
17	1063853	J	24	male	25-03-2019	Head jerks since 8-9 months of age	Father	8	flexor	yes	6	3	On awakening	crying
18	1174287	JS	18	male	04-09-2020	No head control since birth , staring look x few secs since 10 months	Mother	8	flexor	yes	8	2	When drowsy	crying
19	1102483	JK	6	male	17-12-2020	Flexion jerks of upper limbs x 2 months	Mother	4	flexor	yes	4	1	On awakening	crying
20	1322965	K	7	male	11-01-2021	Abnormal body movements x 15 days	Mother	7	flexor	yes	7	4	When asleep	crying
21	1289250	KRS	12	male	04-03-2021	Poor eye contact since birth , flexion spasms of arms x 3 months	Mother	9	flexor	yes	8	2	On awakening	crying

S. NO	MRD NO.	OTHER TYPE OF SEIZURES	VIDEO RECORDED	FAMILY HISTORY	BIRTH HISTORY	GESTATION	BIRTH WEIGHT(kg)	CRY	ANTENATAL PROBLEMS	PERINATAL ILLNESSES	DEVELOPMENT	DEVELOPMENTAL SLOWING OR REGRESSION SINCE ONSET OF SPASMS	WEIGHT (kg)
1	1123620	none	no	none	NVD	Term	2.25	Immediate	none	Hypoglycemia	delayed	yes	10
2	1257090	Tonic clonic seizures	no	none	LSCS	Preterm	2.5	Immediate	none	Prematurity	delayed	yes	18.5
3	1250329	none	yes	none	NVD	Term	2.75	Delayed	none	HIE	delayed	yes	9.4
4	1175116	Tonic clonic seizures	yes	none	NVD	Term	2.5	Immediate	none	Hypoglycemia	delayed	yes	8.5
5	1256454	none	no	none	LSCS	Term	2.75	Immediate	Oligohydramnios	Hypoglycemia	delayed	no	7.5
6	1061850	none	no	none	NVD	Term	3	Delayed	none	HIE	delayed	yes	12.3
7	1130256	Focal seizures.	yes	h/o Epilepsy in paternal uncle	LSCS	Preterm	2.1	Immediate	Hypertension, Overt Diabetes	Prematurity	delayed	yes	8.5
8	1130901	none	yes	none	LSCS	Preterm	2.2	No cry	none	Prematurity	delayed	yes	7.5
9	1146473	none	yes	none	LSCS	Preterm	1	Immediate	Preeclampsia	Hypoglycemia	delayed	yes	8
10	1147261	none	no	none	NVD	Term	2.2	Immediate	none	Hypoglycemia	delayed	yes	10.5
11	1134164	none	yes	none	NVD	Term	4.2	Immediate	none	none	delayed	yes	9.5
12	1102467	none	yes	h/o Epilepsy in cousin brother	LSCS	Term	3	Immediate	none	none	delayed	yes	17
13	1267379	none	yes	none	NVD	Preterm	1.3	Not known	Dengue , UTI, Thick MSL	Prematurity	delayed	yes	4.6
14	1266315	none	no	none	NVD	Preterm	1.9	Delayed	LPV X 3days	Prematurity	delayed	yes	7.7
15	1293940	none	yes	none	LSCS	Term	3	Immediate	none	none	delayed	yes	11.6
16	1164287	Tonic clonic seizures	yes	none	LSCS	Term	1.8	Immediate	MSL	Meningitis	delayed	yes	9.3
17	1063853	none	yes	none	NVD	Term	2.8	Immediate	none	none	delayed	yes	11.5
18	1174287	none	yes	none	LSCS	Term	3.1	Delayed	none	HIE	delayed	yes	8.4
19	1102483	none	yes	none	LSCS	Preterm	3.75	Immediate	none	Prematurity	delayed	yes	7.5
20	1322965	Focal seizures	yes	none	LSCS	Preterm	2.5	Immediate	none	Meningitis	delayed	no	5.3
21	1289250	none	no	none	LSCS	Preterm	1.8	Not known	IVF Conceived pregnancy	HIE	delayed	yes	9.5

S. NO	MRD NO.	LENGTH (cm)	HEAD CIRCUMFERENCE (cm)	GENERAL PHYSICAL EXAMINATION	DYSMORPHISM	NEUROCUTANEOUS SIGNS	SYSTEMIC EXAMINATION	NEUROLOGICAL EXAMINATION	EEG	MRI	GENETICS STUDIES	FINAL DIAGNOSIS
1	1123620	83	45	Lacks eye contact , no fixation	none	none	NAD	NAD	Hypsarrhythmia	NHBI	-	NHBI
2	1257090	90	50	NAD	none	none	NAD	NAD	Hypsarrhythmia	PVL	-	HIE
3	1250329	75	38	Microcephaly	none	none	NAD	NAD	Hypsarrhythmia	HIE	-	HIE
4	1175116	80	38	Sacral dimple +nt , malnoursihed , thin built, Microcephaly	none	none	NAD	Hypertonia	Hypsarrhythmia	NHBI	-	NHBI
5	1256454	86	44	pallor +nt	none	none	NAD	NAD	Hypsarrhythmia	NHBI	-	NHBI
6	1061850	84	47	scalp swelling since 2 months	none	none	NAD	NAD	Hypsarrhythmia	HIE	-	HIE
7	1130256	77	40	Microcephaly +nt ,pallor +nt	none	none	NAD	NAD	Hypsarrhythmia	PVL	-	HIE
8	1130901	68	43	pallor +nt	none	none	NAD	NAD	Hypsarrhythmia	PVL	-	HIE
9	1146473	72	42	pallor +nt	none	none	NAD	NAD	Hypsarrhythmia	PVL + NHBI	-	NHBI
10	1147261	77	44	NAD	none	none	NAD	NAD	Hypsarrhythmia	NHBI	-	NHBI
11	1134164	68	44	NAD	none	none	NAD	NAD	Hypsarrhythmia	Normal study	-	Idiopathic / Unknown
12	1102467	94	41	Microcephaly	none	none	NAD	Hypotonia	Hypsarrhythmia	Lissencephaly	-	Lissencephaly
13	1267379	64	42	pallor +nt	none	none	NAD	Hypertonia	Hypsarrhythmia	PVL	-	HIE
14	1266315	69	39	Microcephaly +nt, Hyperpigmentation +nt.	none	none	NAD	Hypotonia	Hypsarrhythmia	Cerebral Atrophy	-	Nutritional Vitamin B12 Deficiency
15	1293940	91	47	NAD	none	none	NAD	Hypotonia	Modified Hypsarrhythmia	Lissencephaly	-	Lissencephaly
16	1164287	73	43	pallor +nt, microcephaly , AF- small	none	none	NAD	Hypotonia	Hypsarrhythmia	Meningitis	-	Meningitis
17	1063853	80	43	NAD	None	none	NAD	NAD	Hypsarrhythmia	Normal study	-	Idiopathic / Unknown
18	1174287	78	40.5	Microcephaly	none	none	NAD	NAD	Hypsarrhythmia	HIE	-	HIE
19	1102483	66	42	none	none	none	NAD	Hypotonia	Hypsarrhythmia	Normal study	WES-Negative	Idiopathic / Unknown
20	1322965	68	47	slanting eyes , low set ears , Macrocephaly	Dysmorphic facies	none	NAD	Hypotonia	Hypsarrhythmia	PVL	Karyotype - Trisomy 21	Downs Syndrome
21	1289250	76	42	Microcephaly +nt.	none	none	NAD	Hypertonia	Hypsarrhythmia	PVL	-	HIE

S. NO	MRD NO.	INTIALS	AGE OF PRESENTATION (months)	SEX	DATE OF BIRTH	CHIEF COMPLAINTS	NARRATOR	AGE OF ONSET (in months)	TYPE OF SPASMS	CLUSTERING OF SPASMS	NO. OF SPASMS PER CLUSTER	DURATION OF CLUSTER (minutes)	TIME OF OCCURRENCE OF SPASMS	ASSOCIATED SYMPTOMS
22	1360048	PS	24	male	17-08-2020	Abnormal body movements x 1 & 1/2 year	Father	8	flexor	yes	5	2	When asleep	crying
23	1073584	P	5	male	15-10-2020	Abnormal body movements since 3 weeks	Father	4	flexor	yes	3	1	On awakening	crying
24	1361692	G	7	male	16-02-2022	Flexion jerks of arms & upper limbs x 5-7 days	Mother	7	flexor	yes	8	5	On awakening	crying
25	1314230	R	36	female	10-10-2018	Abnormal body movements since 1 year	Mother	24	mixed	yes	15	5	On awakening	vomiting
26	1360074	R	5	male	03-02-2022	Abnormal body movements x 10 days	Mother	5	flexor	yes	20	4	On awakening	crying
27	1289996	S	20	female	26-07-2020	Head jerks x 6 months	Father	14	flexor	yes	8	5	On awakening	vomiting
28	1260668	S	7	male	26-07-2021	Abnormal body movements x 7days	Mother	7	extensor	yes	20	10	On awakening	crying
29	1265339	S	12	male	03-03-2021	Abnormal body movements since 7 months	Mother	5	flexor	yes	4	1	On awakening	crying
30	1362670	SG	42	male	16-12-2019	Flexion spasms of lower & upper extremities x 7 days	Father	42	flexor	yes	12	5	On awakening	crying
31	1024881	TJ	36	male	30-01-2018	Abnormal body movements x 17 days	Father	36	flexor	yes	10	4	When drowsy	laughing
32	1369127	VPS	24	male	09-10-2020	Abnormal body movements x 1 year	Father	12	flexor	yes	4	2	On awakening	laughing
33	1108804	V	8	male	16-08-2020	Abnormal body movements x 1 month	Mother	7	extensor	yes	4	1	When drowsy	laughing
34	1092579	M	36	male	23-01-2018	Abnormal body movements x 1 month	Mother	36	extensor	yes	5	2	On awakening	crying
35	1014633	D	11	male	02-09-2020	Flexion spasms of head x 3 months	Father	8	flexor	yes	5	2	On awakening	crying
36	1147276	H	5	male	04-03-2022	Flexion jerks of head x 3 weeks	Mother	4	flexor	yes	6	2	On awakening	laughing
37	940987	L	12	male	06-01-2019	Flexion spasms x 6 months	Father	6	flexor	yes	4	1	On awakening	crying
38	925537	A	8	male	05-07-2020	Flexion spasms x 1 month	Mother	7	flexor	yes	6	2	On awakening	crying
39	983966	P	4	male	27-02-2020	Jerky movements of arms	Father	4	flexor	yes	8	2	On awakening	vomiting
40	1015488	R	18	male	17-05-2019	Jerky movements x 2 months	Mother	16	mixed	yes	5	3	On awakening	laughing
41	1018240	TK	13	female	21-12-2019	Head jerks x 3 weeks	Father	12	flexor	yes	4-5	2	On awakening	laughing

S. NO	MRD NO.	OTHER TYPE OF SEIZURES	VIDEO RECORDED	FAMILY HISTORY	BIRTH HISTORY	GESTATION	BIRTH WEIGHT(kg)	CRY	ANTENATAL PROBLEMS	PERINATAL ILLNESSES	DEVELOPMENT	DEVELOPMENTAL SLOWING OR REGRESSION SINCE ONSET OF SPASMS	WEIGHT (kg)
22	1360048	Tonic clonic seizures	yes	none	LSCS	Term	2.5	Immediate	none	none	delayed	yes	12.5
23	1073584	none	yes	none	LSCS	Term	2.7	Delayed	none	HIE	delayed	no	7.7
24	1361692	none	no	none	LSCS	Preterm	1.1	Immediate	none	Prematurity	delayed	yes	8
25	1314230	Myoclonic jerks	yes	none	LSCS	Preterm	1.7	Immediate	none	Prematurity	delayed	yes	13.8
26	1360074	none	yes	none	LSCS	Term	2.5	Immediate	MSL	none	normal	no	7
27	1289996	none	yes	Mental retardation in both parents	NVD	Term	3	Immediate	none	none	delayed	yes	10.7
28	1260668	none	yes	none	LSCS	Term	2.5	Immediate	none	none	delayed	no	7.7
29	1265339	none	yes	none	NVD	Term	2.5	Immediate	none	Hypoglycemia	delayed	no	9
30	1362670	Tonic clonic seizures	yes	none	LSCS	Term	3	Delayed	none	HIE	delayed	no	11
31	1024881	none	no	h/o consanguinity	NVD	Term	2.8	not known	none	HIE	delayed	yes	14
32	1369127	none	yes	none	LSCS	Term	2.5	No cry	none	HIE	delayed	yes	12
33	1108804	none	yes	none	LSCS	Term	2.25	Immediate	none	none	delayed	yes	7.5
34	1092579	Focal seizures	yes	none	LSCS	Preterm	0.9	Immediate	none	Prematurity	delayed	no	11
35	1014633	none	yes	none	NVD	Term	2.1	Delayed	none	Meningitis	delayed	yes	7.5
36	1147276	none	yes	none	LSCS	Term	1.6	Immediate	none	HIE	delayed	yes	4.7
37	940987	none	yes	none	LSCS	Preterm	1.8	Immediate	none	Prematurity	delayed	no	8
38	925537	none	yes	none	LSCS	Preterm	2.5	Delayed	none	Prematurity	delayed	yes	7.8
39	983966	none	yes	none	LSCS	Term	3.5	Delayed	MSL	HIE	delayed	no	5.4
40	1015488	none	yes	none	LSCS	Term	2.25	Immediate	none	Hypoglycemia	delayed	no	8.7
41	1018240	Focal seizures	yes	none	NVD	Term	2.3	Immediate	none	Hypoglycemia	delayed	yes	10.2

S. NO	MRD NO.	LENGTH (cm)	HEAD CIRCUMFERENCE (cm)	GENERAL PHYSICAL EXAMINATION	DYSMORPHISM	NEUROCUTANEOUS SIGNS	SYSTEMIC EXAMINATION	NEUROLOGICAL EXAMINATION	EEG	MRI	GENETICS STUDIES	FINAL DIAGNOSIS
22	1360048	86	45	NAD	none	none	NAD	Hypotonia	Hypsarrhythmia	Normal study	-	Idiopathic / Unknown
23	1073584	64	39	Microcephaly , AF Closed	none	none	NAD	Hypertonia	Hypsarrhythmia	HIE	-	HIE
24	1361692	67	44	NAD	none	none	NAD	Hypertonia	Hypsarrhythmia	PVL	-	HIE
25	1314230	96	50	NAD	none	none	NAD	NAD	Hypsarrhythmia	Normal Study	-	Idiopathic/ Unknown
26	1360074	74	42	NAD	none	none	NAD	NAD	Hypsarrhythmia	Normal study	-	Idiopathic/Unknown
27	1289996	85	44	pallor	none	none	NAD	NAD	Hypsarrhythmia	Normal study	-	Idiopathic/Unknown
28	1260668	70	43	Hyperpigmentation over forehead	none	none	NAD	NAD	Hypsarrhythmia	Normal study	-	Idiopathic / Unknown
29	1265339	76	46	NAD	none	none	NAD	NAD	Hypsarrhythmia	NHBI	-	NHBI
30	1362670	84	48	NAD	none	none	NAD	NAD	Modified Hypsarrhythmia	HIE	-	HIE
31	1024881	90	47	NAD	none	none	NAD	Hypotonia	Hypsarrhythmia	HIE	-	HIE
32	1369127	84	43	Brown hair, Microcephaly	none	none	NAD	NAD	Hypsarrhythmia	HIE	-	HIE
33	1108804	72	41	squint +	none	none	NAD	NAD	Hypsarrhythmia	Normal study	-	Idiopathic / Unknown
34	1092579	86	38	Malnourished, Microcephaly	none	none	NAD	Hypertonia	Hypsarrhythmia	Not done	-	HIE
35	1014633	71	43	NAD	none	none	NAD	NAD	Hypsarrhythmia	Meningitis	-	Meningitis
36	1147276	60	40	pallor	none	none	NAD	Hypertonia	Hypsarrhythmia	HIE	-	HIE
37	940987	72	43	NAD	none	none	NAD	Hypertonia	Hypsarrhythmia	PVL	-	HIE
38	925537	74	43	NAD	none	none	NAD	Hypertonia	Hypsarrhythmia	PVL	-	HIE
39	983966	58	38	Small AF, microcephaly	none	none	NAD	Hypertonia	Hypsarrhythmia	HIE	-	HIE
40	1015488	72	40	pallor , Microcephaly	none	none	NAD	Hypertonia	Hypsarrhythmia	PVL	-	HIE
41	1018240	76	43	NAD	none	none	NAD	NAD	Hypsarrhythmia	NHBI	-	NHBI

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Subject: Approval of Plan of Thesis.

This is to inform you that the Faculty of Medical Sciences in its meeting held on 29.10.2021 has approved the plan of thesis of **Amneet Kaur**, a student of your college for **MD Paediatrics** along with the names of Supervisor/Co-Supervisor as under:-

Topic Plan of Thesis

To study the clinical and etiological profile of epileptic spasms in children.

Supervisor
Dr. Jatinder Singh Goraya
Assoc. Prof.,
Dept. of Paediatrics,
DMCH, Ludhiana.

Co-Supervisor

Dr. Siddharth Bhargava, Assoc. Prof.,
Dept. of Paediatrics,
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The student has to submit the four copies of thesis (along with PDF format) , to the Controller of Examinations, BFUHS, Faridkot, at least six months before the commencement of theory examination, if he/she is otherwise eligible to take the examination. He /She must directed to attach a photocopy of this letter with the forwarding letter while submitting thesis to the University along with the letter of approval of University for change of supervisor/Co-Supervisor, change of topic,(if any).

Dr. S P Singh MS(Oph)
Controller of Examinations

Note :

79. *If any discrepancy found regarding topic of thesis or Supervisor/Co-Supervisor, inform undersigned within one month after issue of this letter.*
80. *The student may submit the thesis as per the schedule already conveyed i.e for May/June examination 30th Nov of the preceding the year of examination and for Nov/Dec examinations 31st May of the year of examination.*

TO STUDY THE CLINICAL AND ETIOLOGICAL PROFILE OF EPILEPTIC SPASMS IN CHILDREN

THESIS PROPOSAL

FOR APPROVAL OF SUBJECT OF THESIS TO BE SUBMITTED IN

PARTIAL FULFILMENT OF THE REQUIREMENTS

FOR THE DEGREE OF

MD

In

PEDIATRICS

OF THE

BABA FARID UNIVERSITY OF HEALTH SCIENCES

FARIDKOT

MARCH, 2021

DR. AMNEET KAUR

DEPARTMENT OF PEDIATRICS
DAYANAND MEDICAL COLLEGE AND HOSPITAL
LUDHIANA

ABSTRACT OF PLAN OF THESIS

Title	TO STUDY THE CLINICAL AND ETIOLOGICAL PROFILE OF EPILEPTIC SPASMS IN CHILDREN
For the degree of	MD (Pediatrics)
Name of the candidate	Dr. Amneet kaur
Supervisor	Dr. Jatinder Singh Goraya, Associate Professor, Department of Pediatrics, DMCH, Ludhiana
Co-supervisors	Dr. Siddharth Bhargava, Associate Professor, Department of Pediatrics DMCH, Ludhiana
Institution	Dayanand Medical College & Hospital, Ludhiana
University	Baba Farid University of Health Sciences, Faridkot

INTRODUCTION: Epileptic spasms are defined as sudden flexion, extension or mixed extension-flexion of predominantly proximal and truncal muscles. Epileptic spasms are a specific type of seizure that predominantly occur in infants and young children and are associated with underlying genetic or acquired brain pathology in majority of the cases.

AIM OF STUDY: To study the clinical and etiological characteristics of epileptic spasms in children. To assess the spectrum of electroencephalographic and neuroimaging findings in children with epileptic spasm

MATERIALS & METHODS: Study will be conducted in department of pediatrics at DMCH, Ludhiana. Children older than one month of age, presenting with epileptic spasms will be included in this study

CLINICAL SIGNIFICANCE: To find the clinical and etiological characteristics of epileptic spasms in the current times, which will be helpful in devising and rationalizing better diagnostic, therapeutic and preventive interventions.

KEYWORDS: Epileptic spasms, infantile spasms, hypsarrythmias, west syndrome.

(Signature) Candidate

(Signature) Co-supervisor

(Signature) Supervisor

(Signature) Principal

CERTIFICATE OF FACILITIES AVAILABLE

This is to certify that the facilities for work on the subject of thesis titled **"TO STUDY THE CLINICAL AND ETIOLOGICAL PROFILE OF EPILEPTIC SPASMS IN CHILDREN"** exist in the Department of Pediatrics, DMC&H, Ludhiana and will be provided to the candidate. We will see that the data being included in the thesis is genuine and is collected by the candidate herself under our supervision and guidance.

Supervisor

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Associate Professor
Department of Pediatrics Neurology
DMCH, Ludhiana

Co-Supervisor

Dr. Siddharth Bhargava
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Head of the Department

Dr. Puneet A Pooni
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Department of Pediatrics
DMCH, Ludhiana

Place : _____

Date : _____

APPROVAL PROFORMA
BY
RESEARCH & ETHICAL COMMITTEE
DAYANAND MEDICAL COLLEGE & HOSPITAL, LUDHIANA

Name of candidate	Dr. Amneet Kaur
Department	Pediatrics
Topic of Thesis	TO STUDY THE CLINICAL AND ETIOLOGICAL PROFILE OF EPILEPTIC SPASMS IN CHILDREN
Likely date of appearing in PG examination	May, 2023
Date of enrollment	25th July, 2020
Name of Head of Department	Dr. Puneet A. Pooni
1) Supervisor **2) Co-Supervisor(s)**	Dr. Jatinder S Goraya Dr. Siddharth Bhargava
Signature of Members of Research Committee with Stamp	**Signature of Members of Ethics Committee with Stamp**
Dr. Harpreet Kaur (Professor & Head, Pathology)	Mr. R K Sharma (Legal Expert)
Dr. Jaspal Singh (Professor & Head, Surgery)	Dr. Ramit Mahajan (Associate Professor, Gastroenterology)
Dr. Dinesh Gupta (Professor & Head, Medicine)	Dr. Anu Sharma (Professor, Anatomy)
Dr. Sandeep Kaushal (Dean Academics & Professor & Head, Pharmacology)	Dr. Sandeep Kaushal (Dean Academics & Professor & Head, Pharmacology)
Dr. Gurpreet S Wander (Vice Principal)	Dr. Gurpreet S Wander (Vice Principal & Professor & Head, Cardiology)
	Dr. Gagandeep Singh (Secretary, Ethics Committee Professor & Head, Neurology)

Approved: Yes / No

Dr. Sandeep Puri
Chairperson
Research Committee

Approved: Yes / ~~No~~

Prof. Arvind Malhotra
Chairperson
Ethics Committee

BABA FARID UNIVERSITY OF HEALTH SCIENCES, FARIDKOT

PROFORMA FOR REGISTRATION OF SUBJECT FOR DISSERTATION

1	NAME OF THE CANDIDATE AND ADDRESS	Dr. Amneet Kaur H.No. 4201, Friends Colony, Street no. 2, Jamalpur, Ludhiana
2	NAME OF THE INSTITUTE	Dayanand Medical College & Hospital, Ludhiana
3	COURSE OF STUDY AND SUBJECT	MD- Pediatrics
4	DATE OF ADMISSION OF COURSE	25/07/2020
5	TITLE OF THE TOPIC	To study the clinical and etiological profile of epileptic spasms in children

6. BRIEF RESUME OF THE INTENDED WORK

6.1 NEED FOR THE STUDY

Epileptic spasms, though long recognized, are still a cause of significant morbidity in children. The knowledge of their etiology and pathogenesis is still evolving .Recognized as an age-related epileptic encephalopathy, epileptic spasms have onset between 3 months and 2 years with an estimated incidence of 0.2 to 0.5 per 1,000 live births per year. It is most frequent form of epilepsy in infancy except neonatal and febrile seizures.[1]

Etiologically, epileptic spasms constitute an age dependent epileptic encephalopathy associated with many different underlying conditions. Perinatal hypoxic ischemic brain injury is recognized as the commonest acquired cause of epileptic spasms. Other adverse perinatal events such as meningitis, encephalitis, metabolic brain injury secondary to hypoglycemia, inborn errors of metabolism, congenital TORCH infections are also recognized antecedents of epileptic spasms. Of the genetic etiologies, tuberous Sclerosis, malformations of cortical development such as lissencephaly, polymicrogyria, schizencephaly, and other complex brain malformations are known causes of epileptic spasms.[1-3] With the advent of next generation sequencing, an increasingly number of genes are being identified to as being associated with epileptic spasms in infants and children.

Spectrum of disorders associated with epileptic spasms has undergone significant change over time, attributed to large extent to advances in neuroimaging and genetics, and improved perinatal care. In developed countries, contribution of perinatally acquired brain injury to the causation of epileptic spasms has diminished and that of genetic factors increased. Advances in neuroimaging and genetic techniques has made it possible to recognize increasing role of genetic factors in the etiology of epileptic spasms in these countries.

On the other hand, developing countries such as ours, obstetrical, perinatal and neonatal care still remains suboptimal, perinatal brain injury has emerged as the most common cause of IS in

infants and children in developing countries, even though genetic factors are also increasingly being identified.[4-8] As a result, perinatal risk factors continue to be the dominant cause of epileptic spasms.[4-8] Potentially preventable perinatal causes of neonatal brain injury such as hypoglycemia is being recognized as the most common cause of perinatally acquired etiology of epileptic spasms in Indian children.[8] Paradoxically, genetic factors are also being recognized increasingly, attributable to better availability and affordability of next generation sequencing as well as to improved access to expert pediatric neurological services across the country.[8]

Previously classified as symptomatic, and idiopathic/cryptogenic, epileptic spasms now are classified along with other epilepsies as being structural, genetic/presumed genetic, infectious, metabolic, immune or unknown etiologies. [1-3]

This study intends to find the clinical and etiological characteristics of epileptic spasms in the current times, which will be helpful in devising and rationalizing better diagnostic, therapeutic and preventive interventions.

6.2 REVIEW OF LITERATURE

Epileptic (infantile) spasms were first described by JH West in 1841 in his own son who was healthy until 4 months of age when he developed *bobbings* of head which progressively increased in frequency and severity to cause complete heaving of head towards his knees. The child also suffered from psychomotor retardation.[9]

West syndrome is defined by the triad of epileptic (infantile) spasms, hypsarrhythmia, and psychomotor deterioration, and represents one of the most common catastrophic epileptic encephalopathy with adverse outcome for development and seizure control.[1]

About 100 years later, Gibbs et al. in 1954 described the characteristic electroencephalographic pattern called hypsarrhythmia associated with infantile spasms. It was described by as chaotic and disorganized background activity with asynchronous large amplitude slow waves mixed with single or multifocal spikes and slow waves followed by voltage attenuation.[10] "Modified" hypsarrhythmia pattern with increased interhemispheric synchrony, asymmetry, fragmentation, a consistent focus of abnormal discharge or consisting of only high voltage asynchronous slow activity is also recognized and has same clinical significance as that of classical hypsarrhythmia.[11] Since then, a large amount of scientific literature has accumulated describing clinical, electrographic, neuroimaging, etiological, therapeutic and prognostic characteristics of this peculiar disorder.

Epileptic spasms are defined as sudden flexion, extension or mixed extension-flexion of predominantly proximal and truncal muscles. [12,13] They are generally more sustained than a myoclonic movement but not as sustained as a tonic seizure. Limited forms may also occur: Grimacing, head nodding, or subtle eye movements. Epileptic spasms frequently occur on awakening from sleep and in clusters. Infantile spasms are the best-known form, but epileptic spasms can occur at any age. Consequently, the term "infantile spasm" has been replaced by "epileptic spasms" in the latest International League Against Epilepsy (ILAE) 2017 classification.[12,13] Additionally, infantile spasms

were previously classified as generalized seizures, but now are considered under focal, generalized or unknown onset.[12,13]

Onset of epileptic spasms is during the first years of age in vast majority of the cases with 94% cases occurring within 12 months of age. The most common age of onset is 4–6 months.[14] Occurrence beyond 3 years is extremely uncommon. Slight male predominance has been observed in several studies.[1] The spasms may be flexor, extensor or mixed but the flexor spasms are the most common. [1,3,12]

In a study of 207 infants with epileptic spasms, proven etiology was identified in 61% children.[15] Hypoxic ischemic encephalopathy was the most common etiology and was observed in 21 (10%), followed by chromosomal aberrations in 16 (8%), brain malformations in 16 (8%), stroke in 16 (8%), Tuberous sclerosis complex in 15 (7%) and periventricular leukomalacia / hemorrhage in 11 (5%). Miscellaneous and uncommon etiologies were diagnosed in 32 children. Similarly, in another prospective, multicenter study of 251 children with epileptic spasms, an etiology was established in 161 (64%). Of these, clinical assessment and/or MRI identified an obvious cause in 138 (55%). A genetic cause was identified in 14%, and metabolic in 5% children.[16]

Only few Indian studies on epileptic spasms are available, and most of these studies predate the latest 2017 ILAE classification of seizures and epilepsies.[12] A perusal of these studies revealed symptomatic etiology in more than 80% of the cases with preponderance of perinatal brain injury especially asphyxial hypoxic ischemic encephalopathy in the etiology of infantile spams.[4-8] This is clearly greater than of about 60% reported in the western literature.[15,16]

The etiology is identified in 60 to 75% of cases with relevant radiological, infectious, and metabolic investigations. Neurocutaneous syndromes, brain malformations, neonatal strokes, and sequelae of hypoxic ischemic encephalopathy are often obvious on a magnetic resonance imaging (MRI). Tuberous sclerosis (TS), the most well-

known genetic association with infantile spasms, occurs in only 1 to 19% of children with infantile spasms.[15,17]

Study from AIIMS, New Delhi described 95 children between 1 to 5 years of age who presented with epileptic spasms. Symptomatic etiology was observed in the majority, accounting for 78 (82%) of the cases. Perinatal asphyxia and neonatal sepsis/meningitis were reported in 43 (45%) and 29 (30%) children with epileptic spasms. Other frequent risk factors were brain malformations in 9, tuberous sclerosis in 4, and perinatal stroke in three.[6]

Another study by Singhi and Ray from Chandigarh, North India reported 165 children aged 1.5 month to 4.5 years who presented with epileptic spasms. Age of onset ranged from 1 month to 19 months. Flexor spasms occurred in 74% children. Other type of seizures occurred in 31 children. Adverse perinatal events were recorded in 59%. Tuberous sclerosis contributed to ES in 13 cases.[5]

A recent retrospective study by Kaushik et al. of 148 children (120 boys) with epileptic spasms, described etiological diagnosis in 122 (82%). Perinatal brain injury was identified in 81 (66%) children, with perinatal asphyxia being the dominant cause. Malformations of cortical development in 5, intrauterine infections in 2, tuberous sclerosis in 1 and inherited metabolic disorders in 2 were the other uncommon causes of ES.[7]

More than 60% patients in another Indian study had perinatal insults as the cause of infantile spasms.[18] Worldwide, perinatal asphyxia is a relatively common cause of spasms. Other structural causes can be malformations of brain and cortical development which include – focal cortical dysplasia, polymicrogyria and malformations associated with tuberous sclerosis. In the non-structural group, chromosomal disorders, inborn errors of metabolism and single gene disorders form the major subgroups.[15]

All these studies have established that perinatal brain injury, especially asphyxial hypoxic ischemic injury continues to play a dominant role in the etiology of this devastating epileptic encephalopathy of epileptic spasms. On the other hand, in a recent retrospective study of the 113

children with epileptic spasms from Jaipur India, authors were able to establish a definite etiology in 94 (83%) children. Unlike previous Indian studies, neonatal hypoglycemic brain injury emerged as the most common acquired cause of epileptic spasms and was identified in 40 (35%) children. Asphyxial brain injury was identified in 29 children and was the second most common perinatally acquired cause. Of importance is the finding of genetic etiology identified in 17 children including 5 with tuberous sclerosis and 12 non-tuberous sclerosis gene mutations.[8]

6.3 AIMS AND OBJECTIVES OF THE STUDY

- To study the clinical and etiological characteristics of epileptic spasms in children.
- To assess the spectrum of electroencephalographic and neuroimaging findings in children with epileptic spasm.

7. MATERIALS AND METHODS

The study will be carried out in the Department of Pediatrics, Dayanand Medical College and Hospital, Ludhiana for 15 months from 1st March 2021 to 31st May 2022

Choice of Subjects: Children between than 1 month to 14 years of age with the diagnosis of epileptic spasms defined as sudden occurrence of flexion, extension or mixed, brief and synchronous movement of the head, trunk or limbs, and often occurring in clusters will be studied.

Following inclusion and exclusion criteria will be employed:

7.1 Source of Data

Children attending the pediatric out-patient, in-patient and pediatric emergency who are eventually diagnosed with epileptic spasms will be considered for enrollment.

7.2 METHOD OF COLLECTION OF DATA

INCLUSION CRITERIA:

- Presentation with epileptic spasms
- Age between 1 month to 14 years.

EXCLUSION CRITERIA:

- Parent's refusal to participate in the study.

Written consent will be obtained from the parents of the children with epileptic spasms. The selected children meeting the inclusion criteria will undergo detailed clinical evaluation by history and physical examination. Minimum laboratory investigations will include an electroencephalogram (EEG) and brain MRI. Additional laboratory evaluation will be based on the results of clinical evaluation and neuroimaging findings

Duration of the study: 15 months (from 1st March 2021 to 31st May 2022)

OUTCOME: We will find the etiology and clinical profile of epileptic spasms in children**.**

STATISTICAL ANALYSIS

Data will be described in terms of range; mean ± standard deviation(±SD), median, frequencies (number of cases) and relative

frequencies (percentages) as appropriate. All statistical calculations will be done using (Statical Package for the Social Science) SPSS 21version (SPSS Inc., Chicago, IL, USA) statistical program for Microsoft Windows

7.3 DOES THE STUDY REQUIRE ANY INVESTIGATIONS OR INTERVENTIONS TO BE CONDUCTED ON PATIENTS OR OTHER HUMANS OR ANIMALS? IF SO, PLEASE DESCRIBE BRIEFLY.

Brain MRI and an EEG are the minimum essential investigations which are done in all children with epileptic spasms. Additional investigations, generally blood work, are required in a small percentage (not more than 20%) of children with epileptic spasms

7.4 HAS ETHICAL CLEARANCE BEEN OBTAINED FROM YOUR INSTITUTION IN CASE OF 7.3?

Attached herewith

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PROFORMA

Sr. no

Name : Age/Gender: Date of Birth:

MRD No.: Place of presentation: OPD/IPD/ Emergency

Referring Diagnosis:

Chief complaint:

Duration of symptoms/onset age:

Type of spasms:

Flexor-

Extensor-

Mixed -

Clustering of spasms: Yes/No

Number of spasms per cluster:

Duration of cluster:

Time of occurrence of spasms: On awakening/when awake/when drowsy/when asleep

Associated symptoms: Cry/Smile/laugh/vomiting/others during or after spasms

Signature of candidate **Signature of Supervisor**

Other type of seizures if any: (describe onset, type, frequency)

Any other associated symptoms:

Has someone video-recorded the seizure episodes?

Review of systems:

Family History:

Past Medical History:

Past Treatment:

Birth history: Type of delivery: Cesarian section/Vaginal delivery

Term/Preterm Birth weight

Cry: Immediate/delayed

Antenatal problems if any:

Post-natal Illnesses:

HIE/neonatal hypoglycemia /Meningitis /encephalitis /Stroke/Others:

Development: Normal/Delayed

Development slowing/regression since the onset of spasms

Signature of candidate **Signature of Supervisor**

Development Quotient (DQ)

Examination : Wt Ht HC

General Physical Exam:

Dysmorphism:

Neurocutaneous signs:

Systemic Exam:

Neurological Exam:

EEG: (attach report)

MRI brain (attach report)

Other studies:

Final Diagnosis:

Signature of candidate **Signature of Supervisor**

INFORMED PATIENT CONSENT

Date: _____

I.....D/o, W/o, S/o.....
am willing to participate in the study **"TO STUDY THE CLINICAL AND ETIOLOGICAL PROFILE OF EPILEPTIC SPASMS IN CHILDREN"** The procedure with its complications has been explained to me in local vernacular language. I have fully understood that no special tests and extra expenditure in any form, merely for the purpose of thesis is being carried out. I am free to opt out the study any time without assigning any reason.

.....
Signature of the Witness

Name:

.....
Signature of the patient

Signature of Candidate

Signature of Supervisor

मरीज अनुमति फार्म

तिथि _____

मैं _____ पत्नी/पुत्र/पुत्री _____ निवासी _____ इस शोधकार्य **"TO STUDY THE CLINICAL AND ETIOLOGICAL PROFILE OF EPILEPTIC SPASMS IN CHILDREN"** में भाग लेने के लिए सहमत हूँ। मैं इस शोधकार्य में भाग लेने के लिए अपनी स्वेच्छा से तैयार हूँ। मैं पुष्टि करता/करती हूँ की यह स्वीकृति देने के लिए मुझे कोई आर्थिक प्रलोभन नहीं दिया गया और न ही दबाव डाला गया है। मुझे इस शोधकार्य का उद्देश्य स्पष्ट कर दिया गया है और मुझे यह विश्वास है की यह विज्ञान और मानवता के लाभ के लिए है। मुझे इस शोधकार्य में होने वाले जोखिम के बारे में समझा दिया गया है और मेरी समझ में यह जोखिम बहुत मामुली है।

मैं इस शोधकार्य में भाग लेने के सम्बन्ध में किसी भी समय अपनी अस्वीकृति व्यक्त कर सकता/सकती हूँ और मेरे अस्वीकृति व्यक्त करने का मेरे इलाज पर कोई प्रभाव नहीं पड़ेगा।

_____ _____

गवाह के हस्ताक्षर रोगी के हस्ताक्षर/अंगूठे का निशान

नाम: नाम:

_____

अन्वेषक के हस्ताक्षर

_____

विद्यार्थी के हस्ताक्षर

ਮਰੀਜ਼ ਰਜ਼ਾਮੰਦੀ ਫਾਰਮ

ਮਿਤੀ_____

ਮੈ_____ਪਤਨੀ/ਪੁੱਤਰ/ਪੁੱਤਰੀ_____

ਵਾਸੀ _____

"TO STUDY THE CLINICAL AND ETIOLOGICAL PROFILE OF EPILEPTIC SPASMS IN CHILDREN" ਤੇ ਚਲ ਰਹੀ ਖੋਜ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਰਜ਼ਾਮੰਦ ਹਾਂ। ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਮੈ ਆਪਣੀ ਮਰਜ਼ੀ ਨਾਲ ਤਿਆਰ ਹਾਂ। ਮੈ ਇਹ ਦਸਣਾ ਚਾਹੁੰਦਾ ਹਾਂ/ ਚਾਹੁੰਦੀ ਹਾਂ ਕੇ ਇਹ ਰਜ਼ਾਮੰਦੀ ਦੇਣ ਵਾਸਤੇ ਮੈਨੂ ਕਿਸੇ ਵੀ ਤਰਾਂ ਦਾ ਲੋਭ-ਲਾਲਚ ਨਹੀ ਦਿੱਤਾ ਗਿਆ ਅਤੇ ਨਾ ਹੀ ਕੋਈ ਦਬਾ ਪਾਇਆ ਗਿਆ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਦਾ ਮਨੋਰਥ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਭਰੋਸਾ ਦਵਾਇਆ ਗਿਆ ਹੈ ਕੇ ਇਹ ਖੋਜ ਵਿਗਿਆਨ ਅਤੇ ਮਾਨਵਤਾ ਦੀ ਭਲਾਈ ਲਈ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਵਿਚ ਹੋਣ ਵਾਲੇ ਖਤਰੇ ਬਾਰੇ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਯਕੀਨ ਹੈ ਕੇ ਇਹ ਖਤਰਾ ਬਹੁਤ ਮਾਮੂਲੀ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਦਾ ਢੰਗ – ਤਰੀਕਾ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ।

ਮੈ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਬਾਰੇ ਆਪਣੀ ਰਜ਼ਾਮੰਦੀ ਕਿਸੇ ਵੀ ਸਮੇ ਵਾਪਸ ਲੈ ਸਕਦਾ ਹਾਂ/ ਸਕਦੀ ਹਾਂ ਅਤੇ ਮੇਰੀ ਰਜ਼ਾਮੰਦੀ ਵਾਪਸ ਲੈਣ ਦਾ ਮੇਰੇ ਇਲਾਜ ਤੇ ਕੋਈ ਅਸਰ ਨਹੀ ਹੋਵੇਗਾ।

_____
ਗਵਾਹ ਦੇ ਹਸਤਾਖਰ

_____
ਮਰੀਜ਼ ਦੇ ਹਸਤਾਖਰ

ਮਿਤੀ_____

ਮਿਤੀ_____

ਪਤਾ _____

ਪਤਾ _____

_____
ਨਿਰੀਖਕ ਦੇ ਹਸਤਾਖਰ

_____
ਸਿਖਿਆਰਥੀ ਦੇ ਹਸਤਾਖਰ

PATIENT'S PARENT/GUARDIAN CONSENT FORM

Date: ____/____/____

I .....F/o, M/o .....

R/o .....

am willing to let my child participate in the study entitled Bed **"TO STUDY THE CLINICAL AND ETIOLOGICAL PROFILE OF EPILEPTIC SPASMS IN CHILDREN"**. The procedure with its complications has been explained to me in local vernacular language. I have fully understood that no special tests and extra expenditure in any form, merely for the purpose of thesis is being carried out. I am free to opt out the study any time without assigning any reason. This will not affect my treatment and investigation of my child.

_____	_____
Signature of the Witness	Signature/Thumb Impression of guardian
Name:	Name:

_____	_____
Signature of the Supervisor	Signature of Candidate

ਮਰੀਜ ਦੇ ਮਾਤਾ/ਪਿਤਾ ਦਾ ਰਜ਼ਾਮੰਦੀ ਫਾਰਮ

ਮਿਤੀ __/___/____

ਮੈਂ _____ ਪਿਤਾ/ਮਾਤਾ _____,

ਵਾਸੀ _____

ਆਪਣੇ ਬੱਚੇ ਦੇ ਇਸ ਅਧਿਐਨ ਵਿੱਚ ਹਿੱਸਾ ਲੈਣ ਤੇ ਰਜ਼ਾਮੰਦ ਹਾਂ। ਇਸ ਖੋਜ ਕੰਮ ਵਿੱਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਮੈਂ ਆਪਣੀ ਮਰਜ਼ੀ ਨਾਲ ਤਿਆਰ ਹਾਂ। ਮੈਂ ਇਹ ਦਸਣਾ ਚਾਹੁੰਦਾ/ਚਾਹੁੰਦੀ ਹਾਂ ਕਿ ਇਹ ਰਜ਼ਾਮੰਦੀ ਦੇਣ ਵਾਸਤੇ ਮੈਨੂੰ ਕਿਸੇ ਵੀ ਤਰ੍ਹਾਂ ਦਾ ਲੋਭ-ਲਾਲਚ ਨਹੀਂ ਦਿੱਤਾ ਗਿਆ ਅਤੇ ਨਾ ਹੀ ਕੋਈ ਦਬਾ ਪਾਇਆ ਗਿਆ ਹੈ। ਮੈਨੂੰ ਇਸ ਖੋਜ ਦਾ ਮਨੋਰਥ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂੰ ਇਹ ਭਰੋਸਾ ਦਵਾਇਆ ਗਿਆ ਹੈ ਇਹ ਖੋਜ ਵਿਗਿਆਨ ਅਤੇ ਮਾਨਵਤਾ ਦੀ ਭਲਾਈ ਲਈ ਹੈ। ਮੈਨੂੰ ਇਸ ਖੋਜ ਵਿੱਚ ਹੋਣ ਵਾਲੇ ਖਤਰੇ ਬਾਰੇ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆਂ ਹੈ ਅਤੇ ਮੈਨੂੰ ਇਹ ਯਕੀਨ ਹੈ ਕਿ ਇਹ ਖਤਰਾ ਬਹੁਤਾ ਮਾਮੂਲੀ ਹੈ। ਮੈਨੂੰ ਇਸ ਖੋਜ ਕੰਮ ਵਿੱਚ ਹਿੱਸਾ ਲੈਣ ਦਾ ਢੰਗ-ਤਰੀਕਾ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ।

ਮੈਂ ਇਸ ਖੋਜ ਕੰਮ ਵਿੱਚ ਹਿੱਸਾ ਲੈਣ ਬਾਰੇ ਆਪਣੀ ਰਜ਼ਾਮੰਦੀ ਕਿਸੇ ਵੀ ਸਮੇਂ ਵਾਪਸ ਲੈ ਸਕਦਾ/ਸਕਦੀ ਹਾਂ ਅਤੇ ਮੇਰੀ ਰਜ਼ਾਮੰਦੀ ਵਾਪਸ ਲੈਣ ਦਾ ਮੇਰੇ ਬੱਚੇ ਦੇ ਇਲਾਜ ਤੇ ਕੋਈ ਅਸਰ ਨਹੀਂ ਹੋਵੇਗਾ।

_____ _____

ਗਵਾਹ ਦੇ ਹਸਤਾਖਰ ਮਰੀਜ਼ ਦੇ ਹਸਤਾਖਰ

ਮਿਤੀ _____ ਮਿਤੀ _____

ਪਤਾ _____ ਪਤਾ _____

_____ _____

ਨਰੀਖਕ ਦੇ ਹਸਤਾਖਰ ਸਿਖਿਆਰਥੀ ਦੇ ਹਸਤਾਖਰ

मरीज के माता/पिता का अनुमति फार्म

तिथि ___/___/___

मैं _____ पिता/माता/_____

वासी _____,

अपने बच्चे के इस शोधकार्य में भाग लेने के लिए सहमत हूँ। मैं इस शोधकार्य में भाग लेने के लिए अपनी स्वेच्छा से तैयार हूँ। मैं पुष्टि करता/करती हूँ कि स्वीकृत देने के लिए मुझे कोई आर्थिक प्रलोभन नहीं दिया गया और न ही दबाव डाला गया है। मुझे इस शोधकार्य का उद्देश्य स्पष्ट कर दिया गया है और मुझे यह विश्वास है कि यह विज्ञान और मानवता के लाभ के लिए है। मुझे इस शोधकार्य में होने वाले जोखिम के बारे में समझा दिया गया है और मेरी समझ में यह जोखिम बहुत मामूली है।

मैं इस शोधकार्य में भाग लेने के सम्बन्ध में किसी भी समय अपनी अस्वीकृति व्यक्त कर सकता/सकती हूँ और मेरे अस्वीकृति व्यक्त करने का मेरे बच्चे के इलाज पर कोई प्रभाव नहीं पड़ेगा।

_____ _____

गवाह के हस्ताक्षर मरीज के माता/पिता के हस्ताक्षर

तिथि _____

पता _____

_____

_____

_____ _____

नरीक्षक के हस्ताक्षर प्रत्याक्षी के हस्ताक्षर